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TECHNOLOGY

**Biobots, Roll Out!** p.20

MEDICINE

**Toxins Kick Cancer** p.50

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April 2016

## Science in the NATIONAL PARKS

Inside America's wildest  
research spots p.38

**PLUS**

**Voyager: The Man  
Behind the Mission** p.24

**The Next Painkillers:  
Potent & Addiction-Free** p.32

**Coming to  
Paleo-America** p.70

**BONUS  
ONLINE  
CONTENT  
CODE** p. 5



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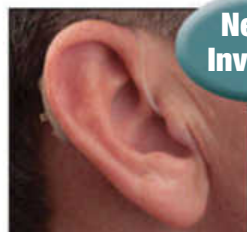
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# Contents

APRIL 2016

VOL. 37, NO. 3

**24** VOYAGER: THE MAN  
BEHIND THE MISSION

## Interstellar Man

For 42 years, Ed Stone  
has led NASA's most audacious  
mission: an unprecedented  
voyage to the solar system's  
farthest reaches. BY COREY S. POWELL

The Voyager 1 probe observed this transit  
of two of Jupiter's moons, Io and Europa.

**ON THE COVER** Photograph by Royce Bair



## FEATURES

### 32 THE NEXT PAINKILLERS: POTENT & ADDICTION-FREE

## This Won't Hurt

Researchers are studying venomous creepy-crawlies in hopes of turning their toxins into potent painkillers without the side effects of current drugs.

BY LEAH SHAFFER

## COVER STORY

### 38 SCIENCE IN THE NATIONAL PARKS

## America's Outdoor Laboratory

A century ago, Congress created the national park system. Today, scientists are using America's "best idea" to better understand the natural world and how we impact it. BY KRISTIN OHLSON

### 50 TOXINS KICK CANCER

## Germ of an Idea

In the 1890s, William Coley destroyed tumors with a risky treatment that sometimes cured — or killed — the patient. But his work led to one of the most promising forms of cancer research: using the human immune system to fight cancer. BY CARL ENGELKING

### 54 Game On

Do winning players rely more on skill, or do they just get lucky? From poker to horse racing, explore the statistics involved in coming out on top.

BY ADAM KUCHARSKI

## COLUMNS & DEPARTMENTS

### 6 EDITOR'S NOTE

## The Only Constant

A change for *Discover*, and a chance to say "thank you."

### 7 THE CRUX

Could aliens be behind one star's crazy light patterns? How can a lotion help diabetics heal their wounds? What does a 3-D-printed violin look and sound like? How can bacteria propel a car? April's Crux answers all of these questions, and more!

### 20 BIG IDEA

## BIOBOTS, ROLL OUT!

## Working Out the Bugs

When it comes to tiny machines, nature already has the best template.

BY SHANNON PALUS

### 60 NOTES FROM EARTH

## Why Are Gray Whales Moving to the Ocean Next Door?

For the first time in thousands of years, gray whales can migrate across the Arctic Ocean to the North Atlantic. But is this new option a good thing?

BY RICHARD SCHIFFMAN



p.32



p.70

### 64 OUT THERE

## A Cosmos, Darkly

Despite being the vast majority of all the matter in the universe, dark matter continues to elude astronomers. But that doesn't mean they don't have a few good guesses. BY COREY S. POWELL

### 70 ORIGIN STORY

## Coming to Paleo-America

Recent genetic studies have ended a decades-long debate over who settled the Americas first, and when. But the studies also pose new questions about those first inhabitants. BY ZACH ZORICH

### 74 20 THINGS YOU DIDN'T KNOW ABOUT ...

## Marijuana

Pot. Cannabis. Mary Jane ... the plant with psychotropic properties has a long pop culture presence — and an even longer record of use. It was one of the first plants used medicinally, and likely one of the first crops grown by the earliest farmers. BY GEMMA TARLACH

# The Only Constant



A change for *Discover*, and a chance to say “thank you.”

In my first editor's note for *Discover*, published almost exactly three years ago, I shared the maxim of one of my favorite science teachers. He liked to say that “change is the only constant in life.” I don't think that he meant to be particularly profound when he said it — usually it was his stock remark to shut up a bunch of whiny high schoolers who objected to learning anything new. I remembered his observation nonetheless and thought it made a good springboard from which to launch my inaugural note to readers.

And now I have to deploy that nugget of wisdom again, because this is my last note to you.

Starting next issue, a new editor in chief, Becky Lang, will have the privilege of connecting with you on this page. Becky is by no means new to the *Discover* team, though, having been a senior editor here for the past few years. A veteran science journalist, Becky came to us from the *Milwaukee Journal Sentinel* where she was part of the editorial team that won the paper a Pulitzer Prize. With Becky, I know that you're in good hands, and will all get along famously.

As for me, I'm not really going all that far. I've taken on new responsibilities with Kalmbach Publishing Co., *Discover's* parent company. I'll still work with Becky and the rest of the team, but this shift does mean that I'm forced to give up one of my favorite parts of the job: filling this page every issue and reaching out to you, our devoted readers.

So while we have this moment alone, I'd like to thank you all for sticking with us, issue in and issue out. And I'm especially grateful to you readers who took time out of your busy schedules to write or call, even if your reasons for reaching out to me weren't always happy ones. You always gave me something new to think about, you often shared insights that improved the magazine, and you never failed to impress me with your passion for science in general and *Discover* in particular. I know you'll share that passion with Becky as she takes the helm next issue.

Stephen C. George, EDITOR IN CHIEF

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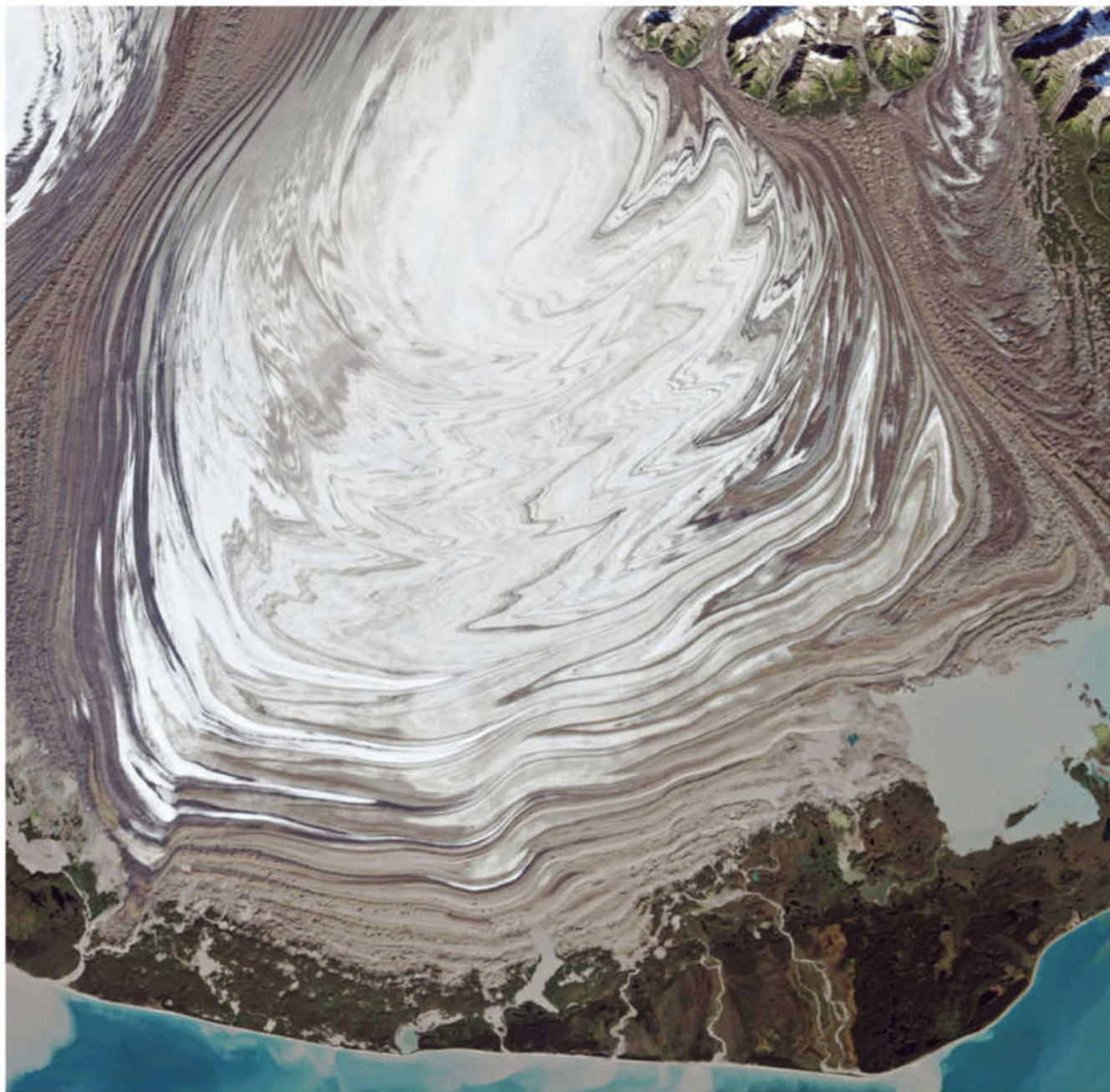






# CRUX

The Latest Science News & Notes



## GLACIER ON THE GO

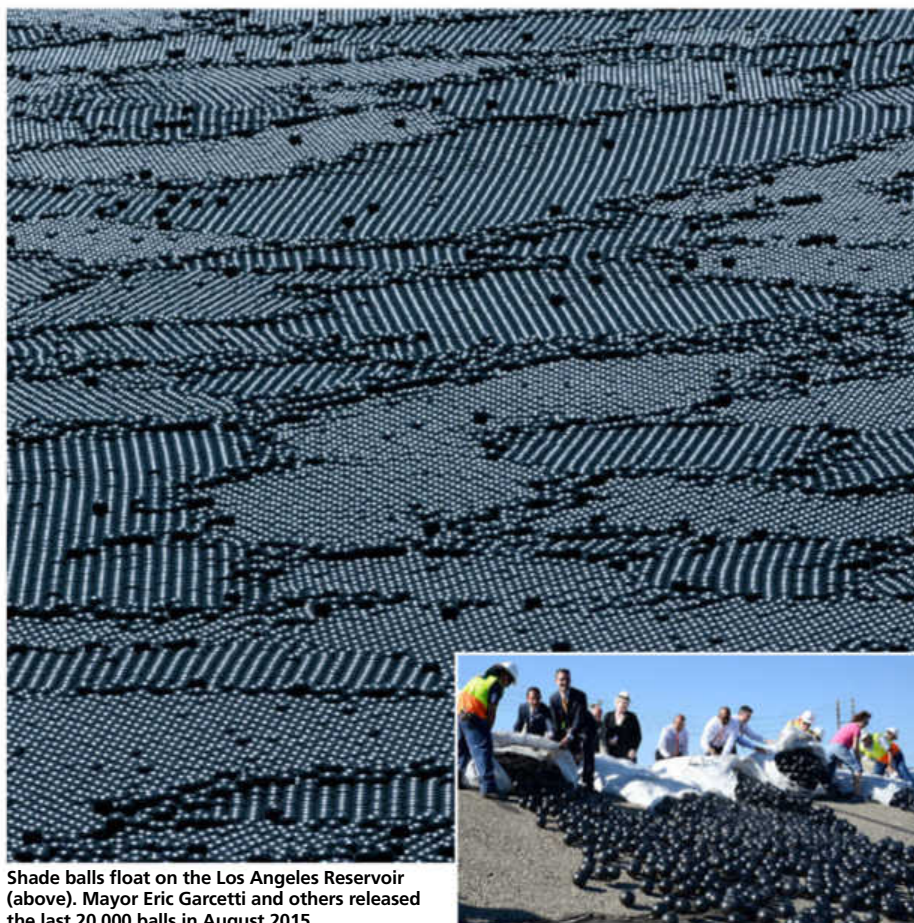
There's nothing wrong with your vision; this is just how Alaska's Malaspina Glacier rolls. Or surges. Those zigzag patterns result from periodic bursts of acceleration in ice flow that can last several years. During a surge, the ice can move 10 to 20 meters per day; the rest of the time, it creeps along at 1 meter or less. As a result, the ice, rock and soil will fold and shear, creating the bold patterns in this 27-mile-wide view from above. The Malaspina is a piedmont glacier, in which the ice spreads out over a wide, flat plain, much like pancake batter in a frying pan. Malaspina is the largest of its type in the world. — ERNIE MASTROIANNI; PHOTO BY NASA EARTH OBSERVATORY/GODDARD SPACE FLIGHT CENTER



# Throwing Shade

Chemistry explains the distinct look of L.A.'s reservoir balls.

**When city officials** placed shade balls in the Los Angeles Reservoir last summer to reduce evaporation and stop sunlight from triggering chemical reactions, onlookers noticed the balls arranging into strangely intricate patterns. Why? Look to chemistry for the answer: The 96 million balls mimic the behavior of atoms. The 4-inch balls are restricted to a two-dimensional plane, so they tend to organize into efficient hexagonal grids, much like the atoms in crystals. Each grid reflects sunlight slightly differently, and lower water levels result in double stacking, leading to the reservoir's patchwork look. —ROBERT COOLMAN



Shade balls float on the Los Angeles Reservoir (above). Mayor Eric Garcetti and others released the last 20,000 balls in August 2015.

## INBOX

### General Confusion

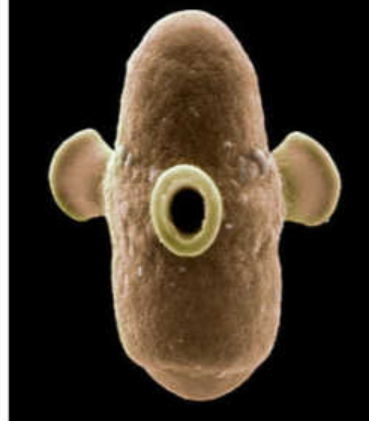
*The December article "The Care and Feeding of Astronauts" mistakenly credited General Mills with the development of Tang. Some readers were quick to correct us:*

*Au contraire; General Mills makes cereals such as Cheerios. General Foods, the premier processed food company of the late 20th century, was the inventor of Tang. It also was responsible for Kool-Aid, Stove Top Stuffing Mix, Jell-O, Post cereals and many other familiar products. General Foods was acquired by Philip Morris in the 1980s and ultimately merged with Kraft Foods.*

**Thomas Parliment** *retired, General Foods Corp., New York*

## WHAT THE...?

Can you figure out what this is? Turn to page 16 for the answer.



## DID YOU KNOW?

Letting someone skip ahead of you in the checkout line? Aren't you nice — though a study in *Human Nature* revealed we're more likely to allow a line-jumper if the benefit to them is greater than our cost, such as waving someone with a few items ahead of you when you're pushing a full cart. Researchers also found, however, that would-be checkout altruists were much less likely to give a pass to someone carrying a bottle of beer. Yes, even in the checkout line we're being judged.



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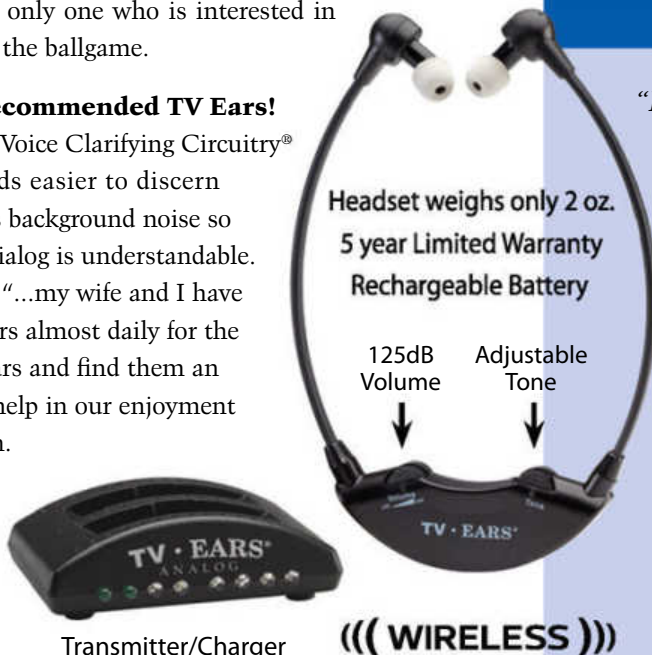
As a retired Otologist,

I heartily recommend TV Ears to people with normal hearing as well as those with hearing loss."

— Robert Forbes, M.D., California

## George Dennis, founder of TV Ears, Inc.

"Driven by my personal understanding of the impact that hearing loss has on a family, I set out to create a product to relieve one of the most frustrating aspects of hearing loss...watching television.



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# Good as Gold

A lotion could heal diabetic wounds.

**A store-bought moisturizer** could become a high-tech remedy for chronic diabetic wounds, thanks to the addition of specialized gold nanoparticles.

Scientists at Northwestern University fortified an over-the-counter lotion with spherical nucleic acids — gold nanoparticles encrusted with the building blocks of DNA and RNA. The team arranged the acids in a specific order to turn off a gene that prevents wounds from healing in Type 2 diabetics.

Standard gene-regulation therapies require painful injections to flip a genetic on-off switch. But with this approach, the team simply applied the lotion to diabetic mice's sores. The nanoparticles infiltrated skin cells, knocked out a gene that produces an enzyme known to interfere with healing, and the wounds closed.

"This is an entirely new approach for treating diabetic wounds," says study co-author and Northwestern dermatologist Amy Paller. The treatment could prevent thousands of diabetic wound-related amputations annually in the U.S.

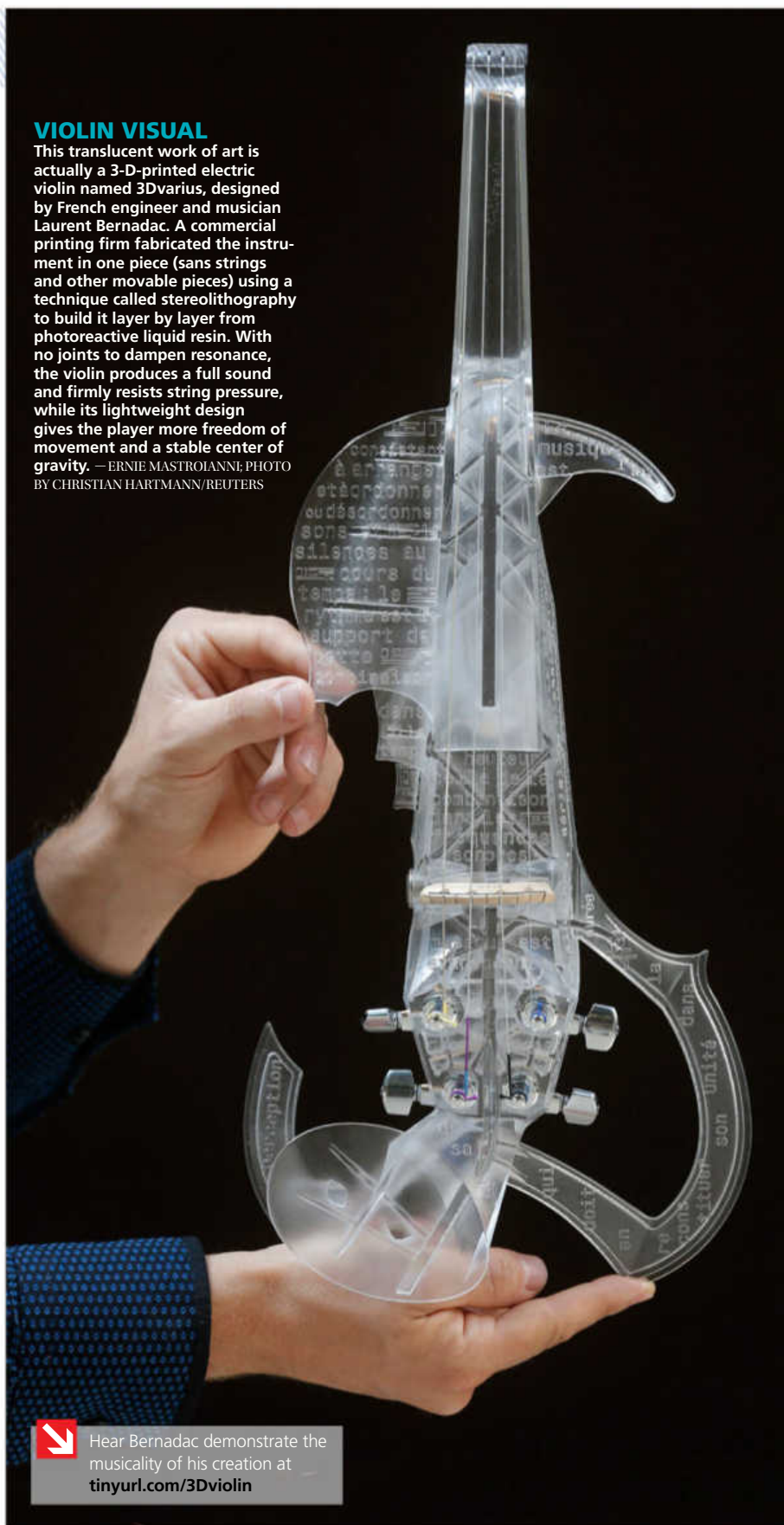
The technique is also customizable and works with most commercial skin lotions. Theoretically, scientists could sequence the nanoparticles to target and treat any of the more than 200 genetically based skin disorders.

—CARL ENGELKING



## VIOLIN VISUAL

This translucent work of art is actually a 3-D-printed electric violin named 3Dvarius, designed by French engineer and musician Laurent Bernadac. A commercial printing firm fabricated the instrument in one piece (sans strings and other movable pieces) using a technique called stereolithography to build it layer by layer from photoreactive liquid resin. With no joints to dampen resonance, the violin produces a full sound and firmly resists string pressure, while its lightweight design gives the player more freedom of movement and a stable center of gravity. —ERNIE MASTROIANNE PHOTO BY CHRISTIAN HARTMANN/REUTERS



Hear Bernadac demonstrate the musicality of his creation at [tinyurl.com/3Dviolin](http://tinyurl.com/3Dviolin)



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# Ask Discover

**Q** What's the deal with that star that was giving off weird light signals? People on the news were suggesting it might be the work of aliens. Seriously? If so, what are the implications for humanity?

— James Praderas, Bellevue, Wash.

**A** The star known as KIC 8462852 does have an unusual light pattern, meaning something odd probably orbits it. Right now, we don't know more than that. Speculation includes a comet swarm or a giant cloud of dust or gas. One other possibility has also captured the media's attention: The star could host a gigantic alien structure.

And this explanation is actually being taken seriously — sort of — by scientists. A study published in December announced SETI scientists had searched the system for laser signals, but they had found none. Still, some remain hopeful of finding other signs of intelligence.

What if astronomers were to find strong evidence that KIC 8462852 is indeed enveloped by an alien megastructure? First, we have to consider that the star resides almost 1,500 light-years away, so what we see is nearly 1,500 years old. That could mean no one's home anymore. Second, there's the public's response. To gauge this, you could ask a social scientist or a sci-fi author.

Social science suggests that knowing a technologically superior alien civilization exists could pose an existential threat for some people, perhaps fundamentally threatening their worldviews or religious beliefs. But this doesn't necessarily mean panic in the



An artist's illustration of an alien megastructure around KIC 8462852. Its light pattern remains unexplained, but aliens probably aren't the cause.

streets, or an end to warfare or religious fanaticism. While some might initially deny the aliens' existence, human beings have usually shown themselves capable of eventually incorporating such a massive paradigm shift into their various belief systems.

Sci-fi author Allen Steele thinks the overall impact on society would be fairly tame. "After a couple of weeks, I think most people would settle back to the way they'd been before," he says, "only now with the awareness that they no longer belong to the most intelligent or powerful race in the known universe." It would be a blow to the ego, sure, but having learned long ago that we aren't the center of the universe, it would be a familiar blow.

—STEPHEN L. ANTCHAK



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This tiny car rolls along with help from an unlikely source.

**A car that runs on bacteria?** It might not be quite the kind of car you're imagining, but researchers report they have built a rotary engine powered by bacterial spores.

A spore lengthens as it soaks up water from the air and shortens with evaporation. To harvest energy from those natural movements, biophysicist Ozgur Sahin and his Columbia University colleagues glued spores to both sides of small tapes, shown in yellow. When dry, the spores make the tapes curl; in humid surroundings, they stretch out.

The team arranged about 100 tapes evenly around a wheel scaffold and encased it in a moist shell that covers half of the wheel. After they rigged it up to a toylike car that weighs as little as a small apple, their contraption, reported in *Nature Communications*, actually propelled the car — albeit at less than 4 inches per minute.

—STEPHEN ORNES

## Here's how it works

1. Moist paper lines the shell's interior. When the water evaporates, it creates a humid chamber.

2. Spores, glued to the tapes, absorb water in the chamber, and the tape lengthens.

3. Here, the spores hang out to dry. When they release the water, the spores shrink, giving extra curl to the tape.

4. The lengthening and curling of the tapes shifts the system's center of mass to the humid side. That shift is the engine's secret weapon: Like an imaginary (and impossible) bicycle wheel on which one side always outweighs the other, it can spin perpetually, so long as there's moisture in the shell. Weights added to the tips of the tapes, shown in blue, bolster the effect.

5. The researchers connected the car's front axle to the big wheel with this rubber belt. As the spores spin the rotary, the belt turns the car's wheels. Vrooom!



To learn more about the car and to see it in action, visit [www.DiscoverMagazine.com/HYDRA](http://www.DiscoverMagazine.com/HYDRA)

**DID YOU KNOW?** Is an after-dinner coffee part of your routine? You may want to reconsider: Drinking the equivalent of a double espresso three hours before going to sleep delays a rise in melatonin, turning back your body clock by nearly an hour, according to researchers from the Medical Research Council Laboratory of Molecular Biology and the University of Colorado.



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## LETTERS

### Dentist Recommends Vinegar

I have some useful advice that others may be interested in. When I got my Dentures several years ago, the Dentist told me use vinegar to get the plaque off them. So - about once a week I soak them in the wonder liquid and Presto - they sparkle.

I have since gotten implants - Since I am not fond of the hygienist scraping the posts for cleaning - I clean them with Vinegar before going for my check-up. On my last visit to her, she couldn't believe how clean they were and praised me for it!

I then asked the Dentist that put the implants in if the vinegar would harm the metal posts and he informed me it is OK to use it.

- D. L., New Braunfels, Tx.

### Vinegar Heals Ear Ache in 2 days.

I have been plagued with an itchy ear for several months. It then developed into an earache. I was able to cure both the itch and earache in two days.

- J. D., Jacksonville, Fl.

### Vinegar Diet helps mother of the Bride

This is kind of embarrassing, but here goes.

My name is Sarah Pierce. I am 58 years old, and through the years (in my mind's eye) I always thought I looked pretty decent.

Especially so when our second daughter was married. I really considered myself a rather 'smashing' Mother of the Bride.

That is, until the wedding pictures came back. I just couldn't believe it.

Here I am, definitely portly - not lean and svelte like I thought. Unfortunately the camera doesn't lie.

Since then, I heard about Emily Thacker's Vinegar Diet and decided to give it a try. What surprised me most was how much I could eat yet I was losing weight and inches. It was like I was getting thin, thinner and thinner yet with the Vinegar Diet. I just thought you should know.

- S. P., N. Canton, Oh.

## NEWS & RESEARCH

### Simple Vinegar used to reduce cervical cancer deaths by 31%

The latest study about vinegar, shows it will prevent an estimated 72,600 deaths from cervical cancer each year.

This according to a study released at the American Society of Clinical Oncology annual meeting in Chicago, IL.

The results were based over a 12 year period tracking 150,000 women in Mumbai, India, between the ages of 35-64 years.

The conclusion, a simple vinegar test significantly reduces cervical cancer deaths. Immediate plans are to implement this simple and successful screening test in developing countries.

The study had been planned for 16 years, but after the results were analyzed and found to be conclusive it was stopped at 12 years.

Vinegar has always been used for its versatility in home remedies, cooking and cleaning. And now scientific and medical findings are showing its a simple, low cost, non-invasive and safe for the patient.

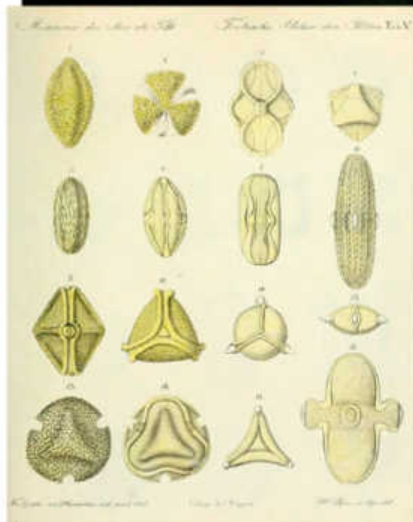
### Scarlett Johansson confesses her apple cider vinegar beauty secret

When celebrity beauty Scarlett Johansson needs to keep her skin looking beautiful and glowing one would think she would turn to high priced beauty creams.

Not so, according to an article in the February 2013 issue of Elle UK. She uses simple apple cider vinegar and its natural pH balancing properties to keep her skin looking amazing.

## WHAT THE...?

It's an individual pollen spore of *Morina persica*, aka prickly whorlflower, photographed via scanning electron microscope. It was one of many spores initially sketched by German pharmacist Carl Julius Fritzsche in 1837.



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## WEB

### Pathologist Pigeons?

In a recent study, researchers showed that trained pigeons could correctly distinguish malignant from benign breast tissue samples that appeared on a touch-screen. With a little more than two weeks of training, the birds' cancer diagnoses were accurate 85 percent of the time. So what did Discover readers think about pigeons' newfound skill?

"They could easily take over my doctor's practice." —Frye H.

"'Bird brain' is not a bad thing anymore!" —September C.

"Uh oh, and I was worried about robots stealing the lab jobs..." —Jessica W.

"Considering the acute senses of many animals, we should be utilizing them in more areas of service. Animals have probably been trying to tell us this all along." —Laurie R.

"Sweet! Now we can pay our oncologists with a bit of popcorn and bread." —Asmarrah B.





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—Katharine, Shreveport, LA

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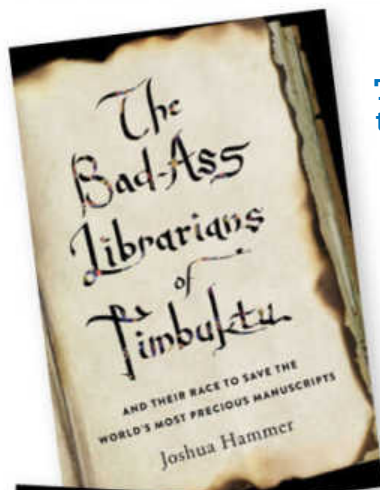
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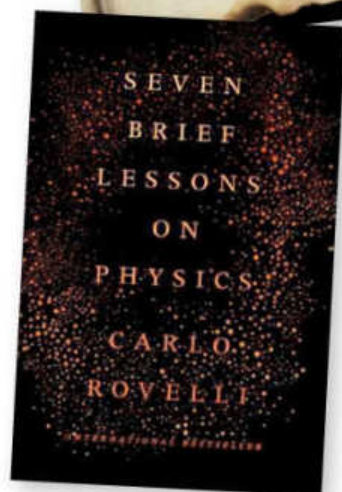
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## THE BAD-ASS LIBRARIANS OF TIMBUKTU and Their Race to Save the World's Most Precious Manuscripts

By Joshua Hammer

While the destructive acts of Islamic extremists worldwide capture headlines, countless stories of heroic resistance rarely receive attention. Award-winning journalist Hammer shines a light on one such episode of bravery and defiance. As al-Qaida advanced on Mali's fabled city of Timbuktu in 2012, a small group of archivists and librarians risked their lives on an elaborate plan to save thousands of rare manuscripts from the marauders. Full of detail about the event and the sociopolitical circumstances leading to it, *Bad-Ass Librarians* also serves as a rousing salute to ordinary civilians who make a stand to preserve cultural heritage against all odds. — ALL REVIEWS BY GEMMA TARLACH



## SEVEN BRIEF LESSONS ON PHYSICS

By Carlo Rovelli

Theoretical physicist Rovelli's essays, which evolved out of a column he wrote for an Italian newspaper, outline the breathtaking "mystery and beauty of the world" with rare skill. His language is accessible and succinct, but it provides an expansive understanding of some of the key ideas in physics — and the questions still bedeviling the field.

## OTHER PAGES WE'RE TURNING

### THE RAREST BIRD IN THE WORLD: The Search for the Nechisar Nightjar

By Vernon R.L. Head

The birder's world is one of intent and patience, an appreciation for the smallest detail and a passion for nuanced description. South African architect Head, a first-time author but a longtime conservationist, dwells in that world. He shares a decades-long story of scientific inquiry bordering on obsession, which was literally built on a wing and a prayer. After a 1990 survey turns up the partial remains — one wing — of a new species, researchers and birdwatchers alike descend on the Ethiopian plain where it was found with the hope of seeing a living specimen.



### STRANGE GLOW: The Story of Radiation

By Timothy J. Jorgensen

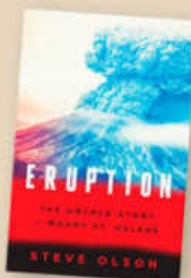
Seen the Internet meme of a black-and-white photo of science supercouple Marie and Pierre Curie in their lab? "You have a certain glow about you, my dear," Pierre tells his wife in the caption. Groan-worthy, sure, but the cheesy pun nails our relationship with radiation, which has been both hero and villain, killer and cure. Jorgensen, a radiation biologist, explores our uncomfortable history with the energy, from life-saving cancer treatments to the deplorable deaths of unsuspecting innocents contaminated by early weapons testing.



### HERDING HEMINGWAY'S CATS: Understanding How Our Genes Work

By Kat Arney

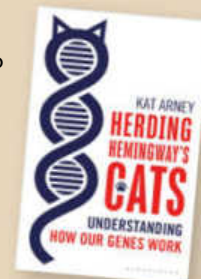
Polydactyl cats have more toes than normal cats due to the flip of a genetic switch, and they've long been considered lucky, especially by mariners and by author Ernest Hemingway, whose home — even well after his death — is still populated with them. Science writer Arney uses the "mitten cat" mutation as a springboard to explain all things DNA in this winning primer on "the cookbook of life." With breezy references to "kick-ass geneticists" and zombies, Arney's book is an entertaining read but never shorts the reader on the actual science.



### ERUPTION: The Untold Story of Mount St. Helens

By Steve Olson

Nearly 36 years after the Pacific Northwest volcano's most famous eruption, Seattle-based writer Olson revisits the event from a new angle. He investigates how the area's history and economy, not just its geology, factored into the deaths of nearly 60 people on that May morning in 1980.





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# Biobots, Roll Out!

When it comes to tiny machines, nature itself already has the best template.

BY SHANNON PALUS

→ You might think of bugs as pests, if you bother to think about them at all. Alper Bozkurt's research will quickly set you straight: To him they're engineering wonders, deft flying and crawling machines that reproduce in nature more reliably than widgets made in a factory.

Bozkurt's interest isn't just academic. By the time his work is through, in maybe 10 years, an army of cockroaches and moths just might save your life.

An electrical and computer engineer at North Carolina State University, Bozkurt is among the first of a kind: He tinkers with bugs. Much of the circuitry he works with already exists — networks of neurons, honed by years of evolution — and he augments this circuitry with his own small electronic devices.

He envisions a future in which “biobots” — bugs with wires that protrude from their bodies and connect to control devices and sensors — serve as rescue teams, listening for cries of help. But they could also be spies surreptitiously listening for secrets, or explorers charting the geology of remote caves. Wherever a bug can crawl, or fly, the biobots could, too.

To make it all possible, these versatile bugs will carry “backpacks,” as Bozkurt describes their payloads. These allow him to control the bugs directly, as well as provide the insect's remote surveillance capabilities, which depend on size. For flying critters — so far just moths — this could just mean routers that allow Wi-Fi signals to pass information and instructions between bugs and mission control. But larger, ground-based cockroaches could carry microphones, gas sensors or anything else a biobot army commander can dream up.



Alper Bozkurt holds a Madagascar hissing cockroach wearing a “backpack” of electronics that allow him to control the bug and see what it sees.

**In the face of such tiny complexity, “we started to have the idea to collaborate with the organisms” instead of starting from scratch.**

Together, the insects form a team that could transform not just search and spy missions, but the very definition of what it means to be a machine.

## HOW TO HACK A MOTH

Many robots take cues from nature, from slithering snake-bots to skittering six-legged (and relatively giant) robo-roaches. But when it comes to micro-flight, mimicking nature is extra difficult.

A separate group at Harvard has worked for years to shrink complex flying mechanisms — a tiny antenna, nervous system, power source — down to a buglike bot as tall as a penny, called a RoboBee. Each individual component warrants scores of journal papers: how it works in nature, how to re-create it mechanically and which materials could

By augmenting living moths (above), scientists can take advantage of nature's designs. Trying to mimic and build them from scratch, like the RoboBee (below), is much harder.



shrink the electronics smaller than ever before. Although RoboBees successfully fly within their lab, their trajectories are pretty unstable; even a small imperfection in its minuscule wings can throw the tiny bot off balance.

In the face of such complexity, “we started to have the idea to *collaborate* with the organisms” instead of starting from scratch, says Bozkurt. As a student a decade ago, Bozkurt worked on microelectromechanical systems, the kinds of sensors that tell your smartphone which way is up and how fast it's moving, for example. Moths, he noticed, are basically an aerodynamic collection of such sensors.

Backed financially by the Defense Advanced Research Projects Agency (DARPA) — a government organization that supports research it hopes will someday be useful to national security — Bozkurt and another electrical engineer raised hawk moths as potential biobot spies. When the moths were pupae in their cocoons, the still-forming tissues could adapt to foreign material, Bozkurt says. He made tiny cuts into the protective shells of the pupae and added three wires into the budding body parts that would soon become the



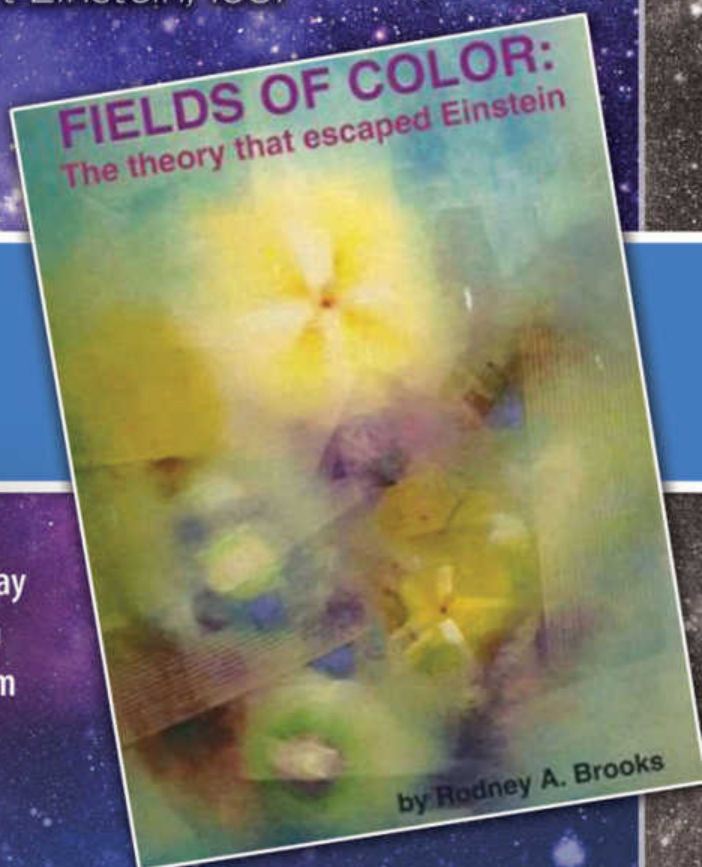


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*-Albert Einstein, 1951*

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brain and neck. A week later the moths hatched, the wires perfectly fused with their brand-new bodies.

In a sense, all creatures — natural, constructed and in between — run on electricity. Take a second to move, or maybe flap, your arms. To accomplish that, your brain had to send an electric signal down the string of neurons in your spine and to the muscles in your shoulders and elbows, telling them to contract and then let go. In the moth, these brain-to-muscle signals flap the wings and tilt the body left or right. Theoretically, if Bozkurt could send the right signals to the moth's neck via the fused wires, he could "drive" the insect.

After attaching a small helium balloon to a moth to balance out the electronics' weight, Bozkurt and Amit Lal, his Ph.D. adviser at Cornell, discovered they really could fly the bug, as if its own brain were sending signals on how to move.

"We made it draw circles [in the air]," says Bozkurt. "Then we were able to bring the insect back down, all by sending the right pulses." There's no struggle — hacking the moth's motions is seamless.

Don't feel bad for the bugs, though; they don't have pain sensors the way that mammals do. When they get a burst of electricity, "they think that this is an environmental stimulus, like a flash of light or a strong scent, and they use their reflexes to follow it or avoid it," Bozkurt suspects. As far as the bugs know, nothing strange is going on, and their lives aren't impacted except when he takes control.

By using this trick, Bozkurt created a bug-sized robot, one that could move better than any purely mechanical device. He just had to co-opt the bug first.

## BACK TO THE GROUND

Of course, even a tiny spy isn't particularly discrete if it's attached to a balloon. DARPA eventually abandoned the idea. After Bozkurt graduated in

One day, an army of roaches may serve as tiny spies, explorers or a rescue team.

## Zaps to the antennae can steer the insect left or right, like a remote-controlled toy.

2010, he set up his own lab at NC State. With support from the National Science Foundation, he turned his attention to implementing his unique electrical skills on cockroaches, and the rescue missions they could go on with their heavier backpacks full of sensory tech. Another benefit: "You can get them at pet stores," says Bozkurt.

He used the same approach — a brief, painless burst of electricity makes the cockroach reflexively change directions. Unlike moths, cockroaches don't go through complete metamorphoses, so Bozkurt couldn't implant electrodes in them while they developed. Instead, he decided to attach them to adult cockroaches' antennae, which they use for sensing their environment.

Once he perfected the new surgical procedure, Bozkurt set off to work, taking advantage of a roach's basic response: Zaps to the antennae can steer the insect left or right, like a remote-controlled toy. First he learned to move the roaches in an S-shaped line. He also confined them to an electronic fence, akin to the fences that jolt pets when they cross an invisible boundary. This lets the roaches mill around as they please while staying within a certain area — useful someday for letting a swarm map an entire area without leaving it.

For the next step, totally automated roaches, Bozkurt connected custom-

made software to a Microsoft Kinect, a motion tracking system designed to play video games without a controller. He could give the software a target that he wanted the roach to move toward. The Kinect's camera tracked the roach's movements, and if it veered away from the target, the software would instantly send an electrical signal to keep the roach moving in the right direction.

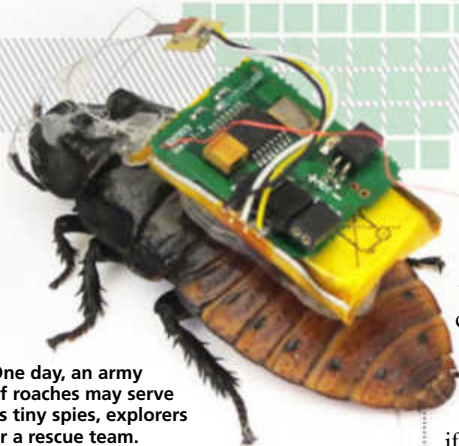
The future army of camera-clad bugs, searching tight spaces for disaster survivors and keeping to a specific route, is that much closer to reality. But in order to deploy roaches in the field, Bozkurt will have to upgrade his sensing system. The Kinect, as a standard camera system, cannot see through ruins or piles of rubble, and it isn't really meant for a space larger than a rec room.

That's why Bozkurt isn't giving up on hawk moths, either. He's collaborating with University of North Carolina biologist Tyson Hedrick to study how moths steer — and how to steer them better. Right now they're "test driving" moths on a custom-built platform: The insect is levitated with an electromagnetic, which holds it in place as it flaps its wings and allows electric signals from a wire to make it orient itself left or right.

When electric payloads have shrunk just a little more, possibly within just a few years, these moths could fly above the roach army sans balloons and relay all the roaches' data, moth-to-moth, back to a base camp. Human operators receiving the roach data, along with the moth's-eye view of the roaches, will guide both species to their next goal.

When the plan becomes reality, a whole new kind of living creature will enter our world: part evolutionary ingenuity, part human genius. But these biobots will also be a new type of machine, perhaps the first of many. The one thing they won't be is a pest. **D**

*Shannon Palus is a writer who lives in Brooklyn, along with the regular cockroaches.*





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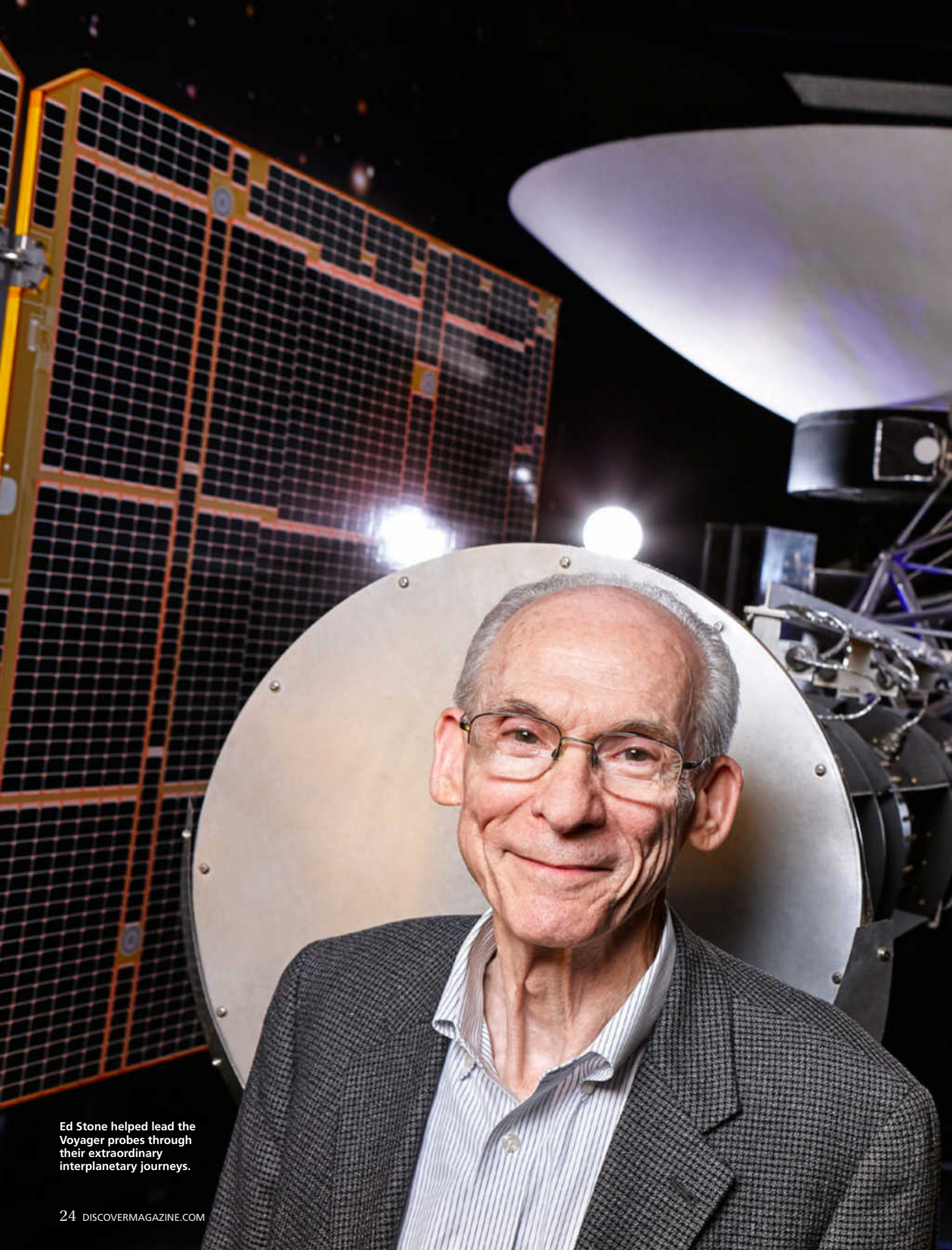
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Ed Stone helped lead the Voyager probes through their extraordinary interplanetary journeys.





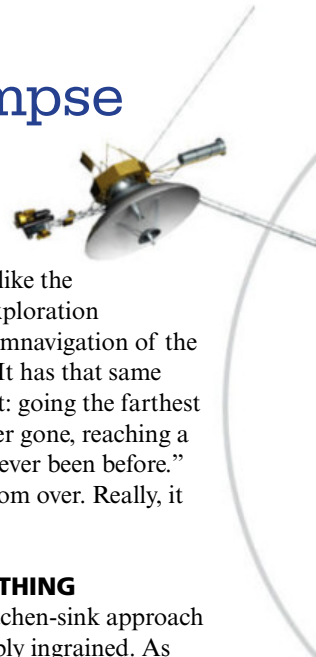
# Interstellar Man

**ED STONE's** relentless pursuit of the frontier has taken him to the edge of the solar system — and beyond.

BY **COREY S. POWELL**

PHOTOGRAPH BY **IAN WHITE**

# Ed Stone is the kind of guy who can glimpse the outer limits of human exploration just by looking at a water faucet.



We are huddled in his minimalist Caltech office, discussing his four decades of work on NASA's twin Voyager space probes. Suddenly he decides that our conversation is getting too abstract. In the summer of 2012, Voyager 1 became the first probe to enter interstellar space, and Stone wants me (and you) to really *feel* what that means. So off we go to a small kitchenette down the hall for a hands-on science explainer.

Everything you need to know about the journey to interstellar space is right there in the sink, Stone explains. He pushes the handle, and a fat stream of water hits the sink's bowl, creating a circular splash. The area within is like the space around Earth and the other planets: a region flooded by the solar wind, a fast-moving outward stream of particles from the sun. The area at the periphery of the sink is like interstellar space, where relatively cold gas between the stars sloshes weakly inward toward us. And in between?

"Notice how a thick ring forms here? That's the termination shock," Stone says excitedly. His finger slowly traces the circle in the sink. The edge between two competing flows of water — one

pushed outward by the faucet's stream and one flowing around the ring toward the drain — mirrors the sharp boundary between the solar wind and the interstellar stream. As in the sink, the boundary takes the form of a shock wave, a dramatic disruption that divides inside from outside (though it spreads in three dimensions, making it into a bubble rather than a ring). That is how Stone knew when Voyager 1 crossed into interstellar space: It passed through a barrier of turbulent particles, like a tiny boat navigating the sink bowl, traversing from inside the circle to outside.

Everywhere Stone looks, he sees frontiers. Over a career that spans the entire Space Age, he has designed some of the first scientific instruments for satellites, directed searches for life-supporting conditions on Mars and above all managed the science team of the Voyager missions that explored Jupiter, Saturn, Uranus and Neptune along with their moons — the single greatest expedition ever undertaken. Now he has transformed *Homo sapiens* into an interstellar species, and at age 80 he has earned a moment to reflect on what he has done.

"There's a historic aspect of these

journeys, very much like the classic journeys of exploration around the first circumnavigation of the Earth," Stone says. "It has that same sort of character to it: going the farthest of anything that's ever gone, reaching a region where we've never been before." But his work is far from over. Really, it never will be.

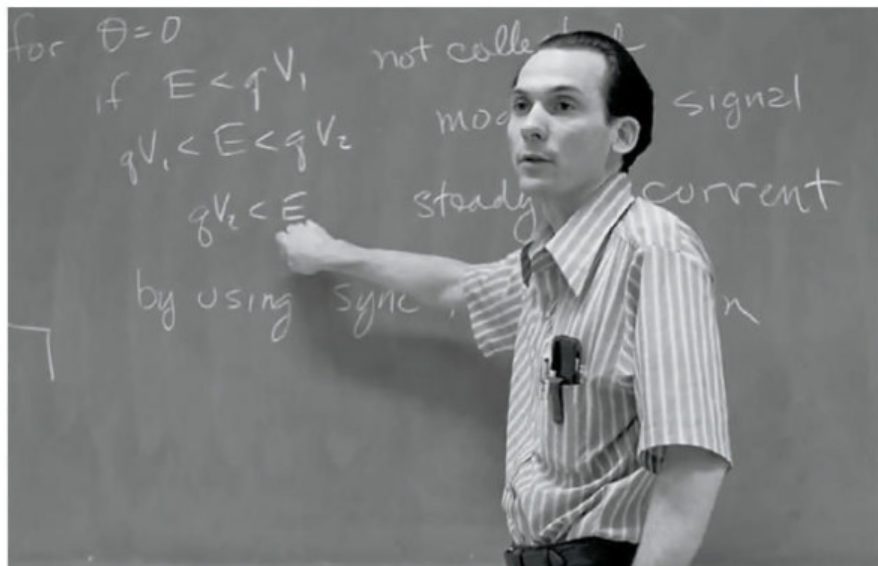
## TIMING IS EVERYTHING

Stone's hands-on, kitchen-sink approach to exploration is deeply ingrained. As a kid in WWII-era Burlington, Iowa, he played with a crystal radio set and tinkered with hi-fi amps. "In those days, that's what you did. Radios were the modern technology," he chuckles. Later he attended the University of Chicago, where he was drawn to nuclear physics — the cutting-edge science of the day — until even newer possibilities intervened.

"I was on my way back to the fall term when I saw the headline that the Soviet Union had launched Sputnik," he says. That was October 1957. By the next summer he was developing ways to study cosmic rays, enigmatic particles that originate from outer space.

Space physics was a wide-open field back then, and Stone's deep familiarity with electronic devices proved a valuable skill. By 1961, he was designing his own cosmic ray detector for the U.S. government. Three years later, he moved to Caltech and co-founded the Space Radiation Lab, where he began some of the earliest studies of solar energetic particles.

Stone had come of age just as NASA was growing rapidly. It had come of age at just the right time, too. In the late 1960s, a group of scientists at the Jet Propulsion Laboratory (a NASA center operated by Caltech) realized that Jupiter, Saturn, Uranus and Neptune were about to fall into a special kind of staggered lineup. A spacecraft could take advantage of the alignment to travel efficiently to all four planets, with each providing a gravitational boost in speed. Such a planetary configuration

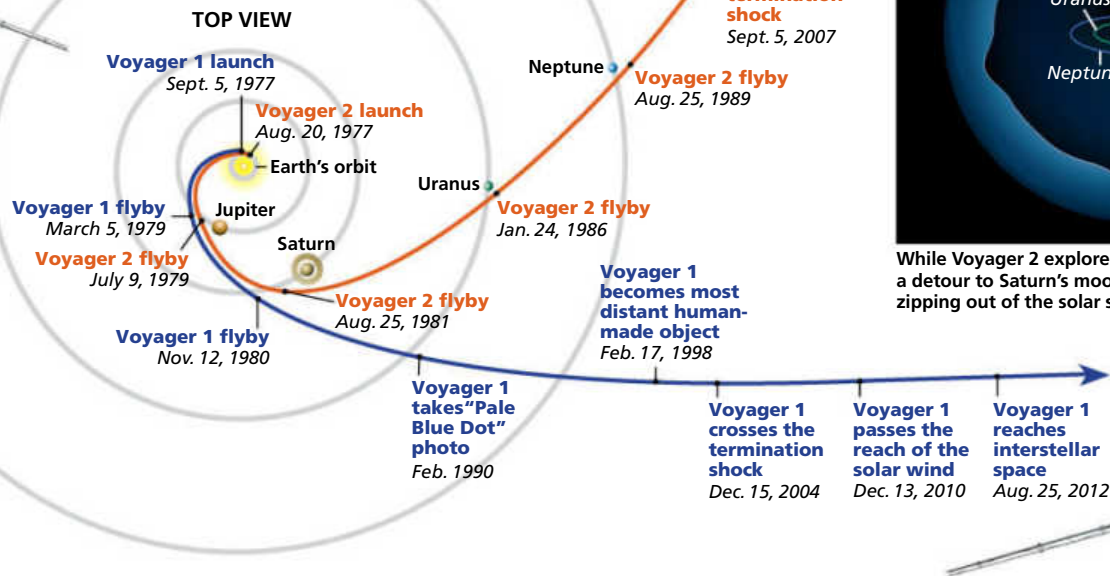


Ed Stone teaches a class at Caltech in 1972, the same year he became project scientist for the planet-hopping Voyager mission.



## THE VOYAGER MISSION

The twin Voyager probes managed to visit all four outer planets, thanks to a kind of alignment that occurs every 176 years.



While Voyager 2 explored Uranus and Neptune, a detour to Saturn's moon Titan sent Voyager 1 zipping out of the solar system at terrific speed.

happens just once every 176 years. In 1972, President Richard Nixon approved sending a pair of identical, redundant spacecraft, Voyagers 1 and 2, to seize the opportunity. Stone became the mission's project scientist, leader of 11 science teams. He was just 36, but he had already built and launched instruments on five different satellites and had no qualms about this huge new responsibility.

Voyager 2 launched on Aug. 20, 1977, and Voyager 1 followed 16 days later, streaking skyward as Stone watched from the control room at Cape Canaveral. (Voyager 1 earned its name because its shorter, faster trajectory meant it would be the first to arrive at Jupiter.)

The twin probes were unlike anything flown before. Each carried 10 separate science instruments, including cameras and devices to measure magnetism and charged particles, along with a state-of-the-art eight-track-tape data recorder and a long-lasting radioactive generator. "These were also the first automated spacecraft that flew themselves," Stone says with justifiable pride. They could take measurements, collect images and even make specific course corrections without instructions from the ground — all with just 1/100,000 the computing

power of a modern smartphone.

After launch, Stone used the 18-month flight to Jupiter as a shake-down period, a quiet time to learn the quirks of his robotic emissaries. Then in March of 1979, Voyager 1 reached Jupiter, and the madness began.

*The twin probes were unlike anything flown before. They could take measurements, collect images and even make specific course corrections without instructions from the ground — all with just 1/100,000 the computing power of a modern smartphone.*

### WORLDS OF FIRE AND ICE

Jupiter is the largest planet in the solar system, with a diverse system of moons, and in 1979 it was nearly unexplored. One of the first and biggest surprises from Voyager 1 was Jupiter's moon Io. In the early images, it resembled a giant pizza and showed not a trace of the expected craters. Meanwhile, attempts to measure Io's temperature kept giving inconsistent, nonsensical results.

The solution came from Linda Morabito, one of Voyager's navigation experts. During an early morning image review, she cranked up the contrast to look for a star she expected to see in the background. Instead, her gaze was drawn to a bizarre, umbrella-shaped

patch of light beside Io. "What's that?" she asked herself. A few hours later, after Morabito and her colleagues had studied the image, they called in Stone to take a look. "His eyes were literally twinkling," she recalls.

Stone instantly grasped what the

scientists were already discussing: The umbrella must be the plume of an enormous eruption, the first sign that Io is the most volcanically active world in the solar system. Conventional wisdom at the time was that moons are small, inert bodies, so the discovery of lava lakes and sulfur jets on Io came as a shock.

"It indicated no matter how much we thought we knew, our experience just was not broad enough," Stone says. Planetary scientists figured out that gravitational interactions with Jupiter and its other large moons create powerful tides on Io, which in turn generates intense heat via friction. That process is now recognized as an important mechanism across the solar system.

## Voyager at Jupiter 483 million miles from the sun



**1:** During its 1979 flyby, Voyager 1 captured Jupiter's Great Red Spot (a feature visible from Earth) and a smaller white spot just below, likely enormous storm systems. **2:** Jupiter's moon Io surprised scientists with a highly geologically active surface. **3:** Fellow Jovian satellite Europa, as seen by Voyager 2, hosts a cracked, icy surface enclosing a warm, possibly inhabited, global ocean.



When Voyager 2 reached Jupiter four months later, the giant planet was once again upstaged by one of its moons. Images of Io's next-door neighbor, Europa, revealed another utterly unexpected landscape: smooth as a cue ball and nearly as white, except for a network of thin, faint brownish fractures. "It just looked like an ice pack," Stone says. More than three

decades later, planetary scientists are still deciphering this enigmatic world.

As on Io, tidal heating has energized Europa. In this case, though, the heat produced not volcanoes but a warm ocean sloshing beneath Europa's icy crust. Today, many researchers consider Europa's inner ocean one of the most likely places to find alien life.

### OVER THE RINGS

After Jupiter came an extended period of tense preparation for the Voyager team. In one sense, not much was happening: the probes were in free flight, slowly making their way across the 500 million-mile gulf to Saturn. But this was a make-or-break moment for Stone and his mission.

NASA had set two key goals for Voyager 1 at Saturn: study the planet's elaborate system of rings and scrutinize its largest moon, Titan, whose composition resembles that of the early Earth. Conducting those observations required that Voyager 1's trip to Saturn would fling it up and out of the plane of the solar system. If all went well, Voyager 2 could take a different path, venturing on to Uranus and Neptune.

But if not, Voyager 2 would take over the primary flight plan, and there would be no extended planetary tour.

Voyager 1 reached Saturn in November 1980. To Stone's excitement, it showed that Titan has a deep atmosphere, thicker than Earth's, full of organic compounds. Thirty-five years later, planetary scientists still marvel over Titan's methane rainstorms and billowing dunes of tar dust. As for the rings, Stone sums them up with two sharp words: "totally bizarre." Voyager 1 observed braided patterns and contrasting spokes that rotated in unison with the planet. The spokes may be caused by electrostatic charges within the rings, but their nature remains mysterious.

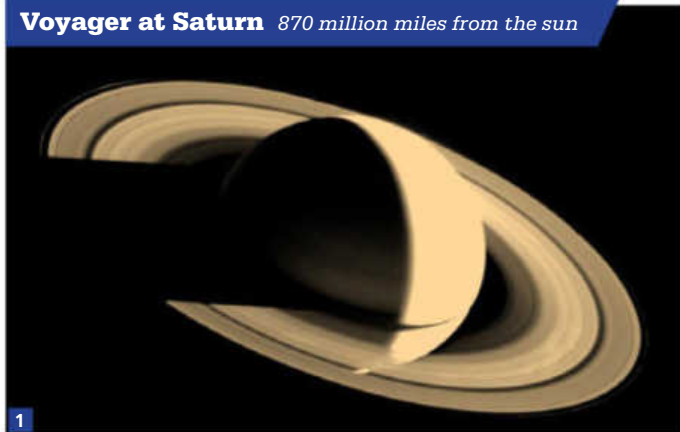
The Saturn encounter was a success, so NASA moved ahead with Plan A: Voyager 1 shot off toward the stars while Voyager 2 set course to Uranus and beyond. But it was hardly smooth sailing. During Voyager 2's Saturn flyby, it lost movement in its scan platform, a turntable that aims the instruments at the correct targets. For the next couple of years, the engineers developed commands that got the scan platform moving again. They also reprogrammed



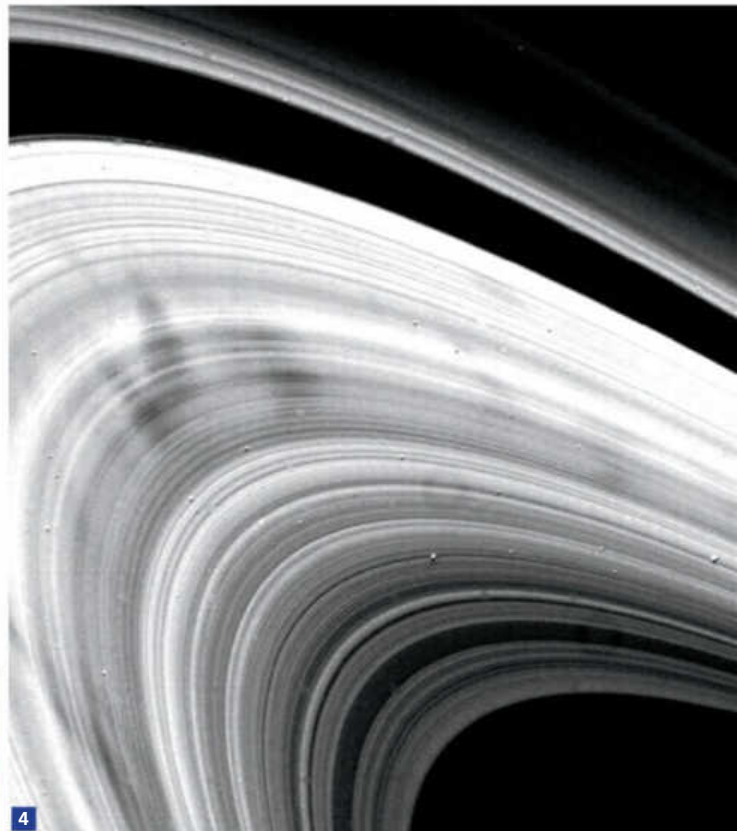
Voyager Project Manager John Casani (left) and Ed Stone pose with a model Voyager probe six months before the real thing's launch.



## Voyager at Saturn 870 million miles from the sun



**1:** Four days after its 1980 flyby, Voyager 1 snapped this rear-facing photo of Saturn and its rings. **2:** The planet's largest moon, Titan, turned out to have an atmosphere thicker than Earth's. **3:** Voyager 1 saw these layers of haze (shown in false color) covering Titan. **4:** Nine months later, Voyager 2 revealed unusual spoke-like structures in Saturn's rings.



Voyager 2 with better ways to take images in the very low light of the outer solar system, and with a more efficient way to transmit data. By the time it reached Uranus on Jan. 24, 1986, Voyager 2 was ready to go.

### THE FINAL PLANETS

Stone's tone turns almost dreamy as he recounts Voyager 2's journey to two completely unexplored worlds.

At Uranus, Voyager 2 found that the planet's magnetic field points sideways, indicating an internal configuration utterly unlike any other planet's. This creates a unique interaction between the planet and the solar wind, a topic of particular interest to Stone. But again, some of the biggest surprises came from the satellites, especially Miranda. "It is only 300 miles in diameter and yet has one of the most complex geological surfaces we've seen," he says — a jumble of mismatched geometric shapes, perhaps from an ancient catastrophe that shattered it into pieces, which later coalesced into the messy moon we see today.

Three years later, in August 1989, Voyager 2 unleashed yet another set

of mind-benders at Neptune. It found winds of over 1,000 mph, the fastest anywhere in the solar system, and dark eruptions on Neptune's largest moon, Triton. "It's the coldest object we visited — it's only 38 kelvins [minus 390 degrees Fahrenheit] — and yet there are geysers," Stone marvels. The geysers evoked Io's volcanoes, but here the activity is powered by frozen nitrogen rather than molten sulfur. That is one of the lasting lessons from Voyager: Even the coldest worlds can be dynamic and complex.

Stone closed out Voyager's planetary adventures as he began, in his focused yet unflappable style. Heidi Hammel, now executive vice president of AURA (the organization that helps oversee the Hubble Space Telescope), was a postdoc working with Stone during the Neptune flyby. "Ed always was a calm spot in the midst of chaos," she says. "I've tried to emulate him: Listen to everyone, synthesize the ideas and present it to the public with joy and wonder."

With Neptune receding, Stone helped guide Voyager 1 to take a look back, creating a panoramic shot of most of the planets lined up around the sun, including the Pale Blue Dot photo of a

lonely Earth. Carl Sagan considered it one of the iconic images of the Space Age. After that, there were no more worlds to visit. The Voyagers raced ahead into the void, and Stone contemplated his next move.

### NEW FRONTIERS

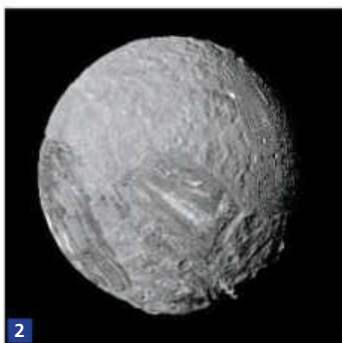
Stone was not idle for long. On Jan. 1, 1991, he took over the entire Jet Propulsion Lab, and he found himself immersed in a space science program struggling with deep budget cuts. If Stone was demoralized, he didn't show it. He gives just a hint of a shrug: "We cannot do everything we're smart enough to know how to do, and it's always a challenge what choices you make."

One tough choice hit him immediately. NASA had been planning a complex pair of probes called the Comet Rendezvous Asteroid Flyby (CRAF) and the Saturn-bound Cassini probe, but their bloated cost was out of line with the agency's post-Cold War budget. President George H.W. Bush canceled CRAF, and Cassini seemed headed for oblivion as well. Stone's team reprised some of the

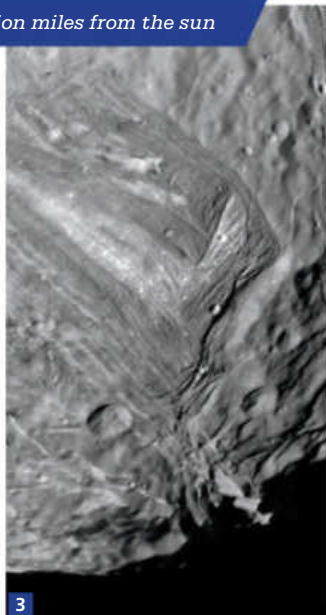
## Voyager at Uranus 1.8 billion miles from the sun



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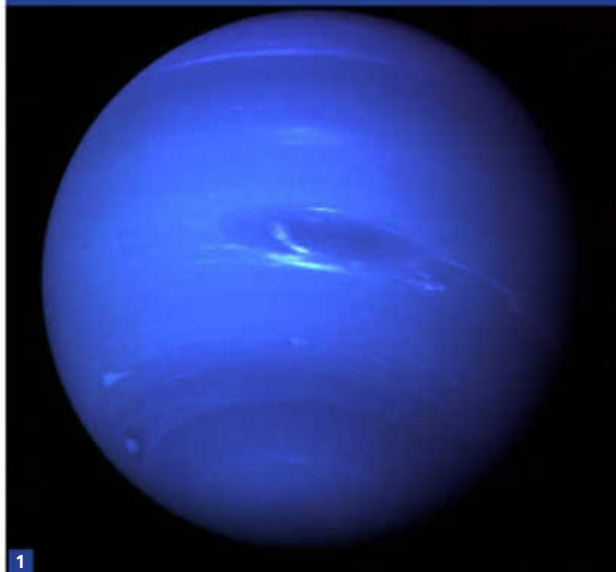
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3

**1:** Uranus was nearly featureless as Voyager 2 sped past in 1986, but sensors picked up the planet's sideways magnetic field. **2:** One of Uranus' smaller moons, 300-mile-wide Miranda, also intrigued scientists. **3:** Its complex and jagged surface may be the result of a long-ago collision, but even today it remains a mystery.

## Voyager at Neptune 2.7 billion miles from the sun



1



2

**1:** Voyager 2's final planet, Neptune, looms large in this photo taken just 4.4 million miles away. The Great Dark Spot and its companion bright smudge were home to some of the fastest winds anywhere in the solar system. **2:** Triton, its largest moon, has a geologically active surface fueled by cryovolcanism.

tricks developed by the Voyager team to make the probe radically simpler and cheaper, "and we didn't lose any part of the science package," he says. Cassini launched in 1997 and still makes stunning discoveries about Saturn and its moons.

Carolyn Porco, Cassini's lead imaging scientist and another of Stone's Voyager-era disciples, credits him with being a model leader. "He was respect-

ful and fair and never, ever arrogant or condescending," she says. "Everyone loved Ed. We should all be like him, enthusiastic and enjoying every opportunity that life has to give."

The other signature mission from Stone's days as JPL director is Mars Pathfinder and its little rover, Sojourner, which landed in 1997. Pathfinder served two important functions, he notes: "It was part of learning how to do things

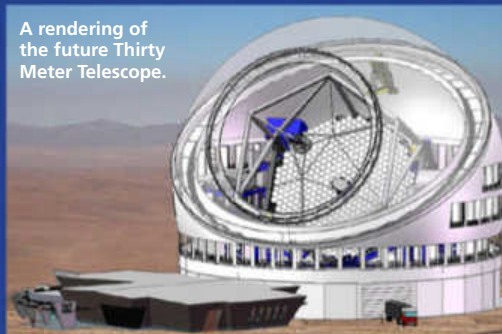
on a smaller scale, and how to rove on the surface of Mars — because you're unlikely to land on the most interesting location." Sojourner's mobility became the template for the successor Mars rovers: Spirit, Opportunity, Curiosity and the upcoming Mars 2020. Stone points out that Pathfinder was also the first NASA mission that became an Internet sensation. "For the first time, it was possible for the public to engage whenever they wanted to," he says.

Stone stepped down from JPL in 2001, but his touch remains in the current cadence of Mars exploration, alternating between big-budget missions like Curiosity and smaller ones like the MAVEN orbiter, which studies the Martian atmosphere.

## FROM HAWAII TO THE EDGE OF HEAVEN

What do you do after pushing the boundaries of the solar system? How about looking to the edge of the cosmos? Stone has signed on as executive director of the Thirty Meter Telescope (TMT), an observatory to be built in Hawaii. The scope will feature a 30-meter (100-foot) light-collecting surface designed to achieve three times the resolution of the Hubble Space Telescope. The TMT was to be completed in 2024, but local groups have protested its location because they regard it as sacred ground; last December, Hawaii's Supreme Court revoked TMT's construction permit. "We are assessing our next steps forward," Stone says. He knows too well that great acts of exploration can't be rushed. —CSP

A rendering of the future Thirty Meter Telescope.



## TO THE EDGE AND BEYOND

Once Stone was free of his director's duties at JPL, he could again focus on the Voyager probes, both now headed inexorably to interstellar space. Their targets were no longer planets but the particles and fields that define the sun's outer environment. Ever since the 1990s, team scientists had been waiting to reach the termination shock — the



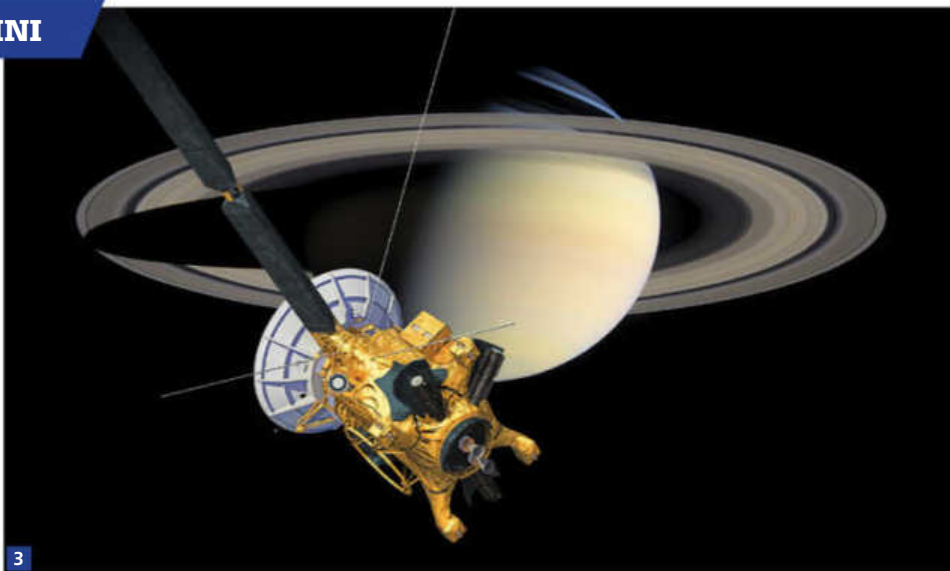
## PATHFINDER & CASSINI

**1:** The Sojourner rover, part of the Mars Pathfinder mission, landed in 1997.

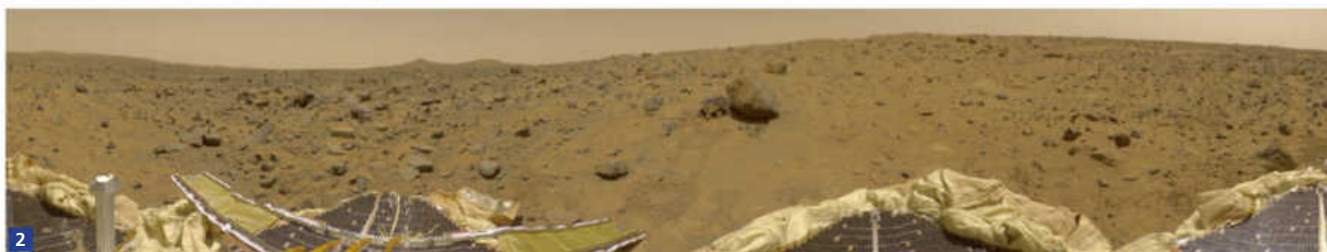
**2:** The mission's photos, such as this one of Sojourner inspecting a boulder near the landing site, were uploaded nearly instantly to the nascent Web. **3:** The same year, NASA launched the Cassini-Huygens mission to study Saturn and Titan. The Cassini probe remains in active service to this day.



1



3



2

boundary that Stone modeled for me in his sink, where the 250-mile-per-second solar wind plows into interstellar material moving less than a tenth as fast. The sudden slowdown should be accompanied by a distinctive pattern of radio signals and particle flows, but detecting it was no simple matter.

As the faster of the two probes, Voyager 1 was poised to reach interstellar space first, but its instrument for measuring the solar wind had stopped functioning in 1980. That forced Stone and his colleagues to rely on indirect evidence, leading to a difficult series of efforts to determine when the craft had truly crossed over.

According to Stone, Voyager 1 reached the termination shock in December 2004, at a distance of 9 billion miles from Earth. Voyager 2, pointing almost 90 degrees away from its twin, hit the shock in 2007 at a distance of just under 8 billion miles. Evidently the sun's outer boundary

layer is lopsided. Piling on the confusion, the termination shock still doesn't qualify as true interstellar space because it is thoroughly blended with the solar wind. Stone watched over the readings from the Voyagers' remaining five active instruments, waiting for the momentous entry into the undiluted interstellar

influence extends far beyond the solar bubble, all the way to the edge of the Oort Cloud some 9 trillion miles away — and Voyager 1 won't get there for 400 more centuries.

For a moment Stone seems frustrated, but a moment later he's eagerly discussing his next projects: He is

*At long last, in 2013 all the data were in, all the disputes were settled. Voyager 1 officially entered interstellar space on Aug. 25, 2012. Let that stand as the day humans became an interstellar species.*

flow. And waiting some more.

At long last, in 2013 all the data were in, all the disputes were settled. Voyager 1 officially entered interstellar space on Aug. 25, 2012. Let that stand as the day humans became an interstellar species.

It's hard to imagine a more extreme territory to conquer, but Stone sounds as restless as ever. "We're outside, but we're still not out in pristine interstellar wind. We're just barely into interstellar space," he says. "And we don't actually leave the solar system for another roughly 40,000 years." He means that the sun's gravitational

helping to build the world's largest telescope, which will scrutinize distant galaxies, and serving as adviser on a space probe that will dive closer to the sun than ever before. After 56 years, Stone is still working full time, seeking out frontiers as methodically as ever.

No plans to retire, then? He offers a half-quizzical, half-smiling look. "My job is my relaxation, really. I'm very lucky." ■

**Corey S. Powell**, a contributing editor of *Discover*, also writes for the magazine's *Out There* blog. Follow him on Twitter: [@coreyspowell](https://twitter.com/coreyspowell)



Explore the scientific instruments aboard the Voyager probes at [DiscoverMagazine.com/Voyager](http://DiscoverMagazine.com/Voyager)



# THIS WON'T HURT

Venomous critters  
may inspire the  
next generation  
of **PAINKILLERS**.

BY LEAH SHAFFER

BIOCHEMIST Glenn King  
researches how to  
turn spider venom  
into a potent painkiller  
at the University of  
Queensland in Australia.

MARK CALLEJA/NEUSPIX





**BIOCHEMIST GLENN KING** spends his days getting up close and personal with the creatures that make us shudder: spiders, centipedes and scorpions. He's collecting their often-deadly venoms to find the perfect painkiller.

King, a researcher at the University of Queensland in Australia, studies the neurotoxins that allow these creatures to paralyze and kill their prey. The toxins shut down a channel on the membranes of different types of neurons. In humans, the same mechanism that spells doom for prey could be modified to stop pain signals in their tracks. As King explains it, this channel is the first step in the process of amplifying pain signals up the spinal cord to the brain. If researchers can use venoms to develop a drug that blocks this channel, we could provide relief for chronic pain sufferers and possibly shake our dependence on opioid-based painkillers, such as oxycodone or hydrocodone.

Derived from the opium poppy, opioids alleviate pain by binding to opioid receptors in the brain. They've been around for thousands of years in one form or another, both as recreational drugs and as painkillers, like morphine or codeine. Along with pain relief, opioids offer euphoria, but they also pose a risk of addiction and drug tolerance.

"It's not simply that they're really addictive, which makes putting someone with chronic pain on an opioid a bad idea. It's also a bad idea because when you take an opioid on a regular basis, they can become ineffective," says Andrew Kolodny, director of Physicians for Responsible Opioid Prescribing, a national advocacy group.

Since the resurgence of opioid-based medications to treat pain in the 1990s, the drugs have become the primary source of fatal overdoses

**By studying different animal toxins, scientists are gaining greater insight into how pain works in the first place.**

in the United States. Seventy-one percent of the 22,767 deaths related to pharmaceutical overdose in 2013 involved prescription opioid pain relievers, according to the Centers for Disease Control and Prevention.

Animal toxins can alleviate chronic pain without inducing tolerance or addiction because they target parts of the nervous system outside the brain. It seems counterintuitive that something meant to kill or paralyze could ultimately save lives, but by studying different toxins produced by animals, scientists are gaining greater insight into how pain works in the first place. In fact, one of the first clues to understanding how pain signals make it to the brain came from an unusual source: snails. But we're getting ahead of ourselves. First, let's look at just *how* we feel pain.

### **PAIN AMPLIFIER**

A pain signal is just your body's way of alerting you to damage in your cells. Cells respond to a threat by leaking a small sodium-ion charge through a pore in the cell membrane called voltage-gated sodium channel 1.7, or Nav 1.7. In effect, this sodium channel amplifies the pain signal so it can be "heard" by the brain, says King.

Researchers confirmed the effects of this channel a decade ago when a doctor from the United Kingdom visited Pakistan. The doctor heard about a street show where a young man could stab himself in the arm without pain, getting patched up later in a hospital. Intrigued, the doctor, a geneticist named Geoffrey Woods, eventually discovered two families who carried a genetic mutation that blocked the functioning of sodium channel 1.7. He found a mutation that kept people pain-free.

Aside from a diminished sense of smell, people with the mutation were otherwise healthy. Woods

published his findings in 2006 in the journal *Nature*, suggesting that this discovery could "stimulate the search for novel analgesics that selectively target this sodium channel."

And that's just what researchers and pharmaceutical companies are racing to do. They want to find something — an engineered small molecule, antibody or, in King's case, a peptide isolated from venom — that inhibits the functioning of sodium channel 1.7. But there are nine similar sodium channels responsible for a variety of functions in the body. For instance, sodium channel 1.5 is the heart sodium channel. If your 1.7-blocking painkiller also blocks 1.5, the patient would die of heart failure, says King.

Most drugs on the market today are small molecules, active organic compounds with a structure and weight so minute that they can be ingested and pass more easily through cell membranes. Many small-molecule drugs work by blocking the pore of a channel, but there's a problem: The pores of all nine sodium channels are similarly shaped.

King believes that venom-based peptides — short chains of amino acids — are better at being selective than small molecules because the venom peptides don't target the pore; they target a specific sodium channel switch. When researchers talk about channel selectivity, they're referring to the ability of peptides or small molecules to turn off only one particular sodium channel.

"Without [sodium channel] 1.7, the pain signals simply don't get amplified to a level where it gets the signal up to the spinal cord and up to the brain," so the brain never knows about it, he says.

**OPIUM**, derived from poppies, has been used for millennia as a potent but addictive source of pain relief.



LEFT: JAVED TANVER/AP/GETTY IMAGES. BELOW: BASTIAN RAST





**HARVESTING VENOM** is easier when working with larger spiders, which secrete the toxin — then collected noninvasively with a pipette — in sufficient amounts for researchers to analyze and test.

## SPIDERS, CENTIPEDES AND SCORPIONS

Not just any venomous creature will do to create sodium channel blockers. “The animals that we’re solely focused on are those that have neurotoxin venoms,” says King.

Snake and reptile venoms typically don’t work for this type of research because most of them function as hemotoxins (which destroy red blood cells) and target components of the cardiovascular system, King says. “You want animals that make molecules that modulate the nervous system.”

To that end, King has collected samples of venom from all over the world, mostly from spiders. “Spiders have proved to be the best so far,” says King, who has screened 300 different arachnid venoms. The more diverse his venom collection, the more likely he can find a useful — and selective — peptide.

Another reason why he works primarily with spiders is that despite their reputation, spiders are not as dangerous to humans. “Even the very biggest tarantula — as big as a dinner plate — can’t kill you,” says King.

For King’s purposes, bigger spiders have another advantage: Their size makes it easier to get sufficient venom to test, compared with smaller species.

Spiders don’t have a monopoly on promising peptides, though.

For millennia, the Chinese have made use of the medicinal properties of



**AUSTRALIAN TARANTULAS**, half a dozen species from four different genera, are among hundreds of arachnids with venom being tested for future painkiller development.

**THE CHINESE RED-HEADED CENTIPEDE**, or *Scolopendra subspinipes mutilans*, has a component in its venom that’s a more potent painkiller than morphine.



scorpion venom for chronic pain and a host of other ailments. Recent research shows that scorpion venom, too, can be a potent sodium channel blocker. King has also found a potential 1.7 blocker in centipedes. In a recent paper published in *Proceedings of the National Academy of Sciences*, King detailed how, in mouse models, a peptide from the venom of the Chinese red-headed centipede acted as a more potent painkiller than morphine — without side effects.

King acquired enough of that centipede for limited testing, but getting sufficient amounts of venom from other species of centipede has proven to be a challenge. “We’re trying to understand how to engineer the venom peptides so they can be even more selective, but to accumulate enough venom to do a screening is very difficult,” he says.

## THE CONE SNAILS

While growing up in the Philippines, biochemist Baldomero Olivera collected the shells of cone snails — small, tropical marine snails whose harpoonlike hook snags and paralyzes fish. Years later, he decided to investigate the chemical components of the snail toxins, which, in rare cases, can cause human fatalities.

In the late 1970s, while at the University of Utah, Olivera’s students Craig Clark and Michael McIntosh tried injecting the cone snail venom directly into the brains of mice and discovered that different components of venom changed

**SCORPIONS** have been valued in China for thousands of years for their venom’s painkilling potential.



**What makes cone snail venom a uniquely useful treasure-trove of potential painkillers is the nature of the snails' attack.**

the animals' behavior. Some made them sleep, jump or even scratch.

Further research determined that certain components of the cone snail venom, called conotoxins, targeted voltage-gated calcium channels, which, like sodium channels, handle communication between pain-sensing neurons and the brain. The colorful snails yielded the first hint that these calcium channels could make a potent target for pain relief. By 2004, the drug companies Neurex and Elan had developed an alternative to morphine called Prialt, or ziconotide, which makes use of this toxin. The downside: The drug has dose-limiting side effects and can be applied only through injection into the spinal cord, making it less practical as a mainstream painkiller.

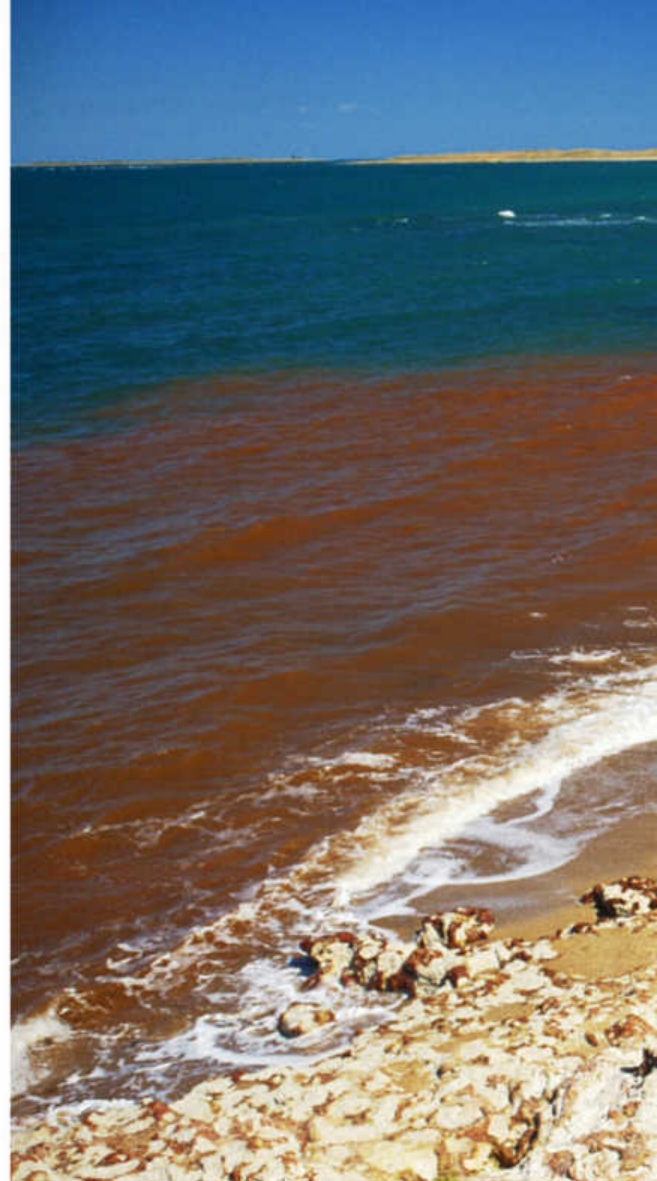
Olivera is still exploring the chemical cocktail available in conotoxins. What makes cone snail venom a uniquely useful treasure-trove of potential pharmaceuticals is the nature of the snails' attack.

To capture prey, predators use mechanical or chemical methods. For instance, a snake has venom, but it also can make use of its speed and jaws to catch prey. Cone snails are tiny creatures without much weaponry to kill besides their venom. "They're totally dependent on having a really potent chemical strategy," says Olivera.

The cone snails have evolved a particularly effective venom, notes chemist David Craik. Their venom peptides hit a wide variety of pain targets, including sodium channels, calcium channels and other receptors.

The challenge of using peptides as drugs is that they're not viable in pill form because our digestive system breaks them down. That's a reason why ziconotide must be injected directly into the spine. But Craik, a researcher at the University of Queensland, is creating drugs based on cone snail toxins that could be taken orally. He's studying a type of plant peptide with a looped structure of amino acids. The loop shape allows the peptide to be more stable — and possibly survive a trip through the digestive tract.

Craik's idea is to combine this type of amino acid structure with a conotoxin, designing a more user-friendly medication, perhaps in pill form. The



**CONE SNAILS** such as this marble cone (*Conus marmoreus*) use a venomous, harpoonlike hook to snag and paralyze small fish.



type of conotoxin molecule he's studying binds to a receptor called GABA B, inhibiting transmission of nerve impulses. Because GABA B is in a different class from opioid receptors, potential side effects in such a drug would be limited.

Conotoxin doesn't act in the central nervous system, which is where you'd worry about serious side effects, says Craik. Instead, it operates in the peripheral nervous system, outside the brain and spinal cord. "It's a different mechanism of action," says Craik, who has tested the new drug in animals and hopes to begin human trials within two years.

## UNDER THE SEA

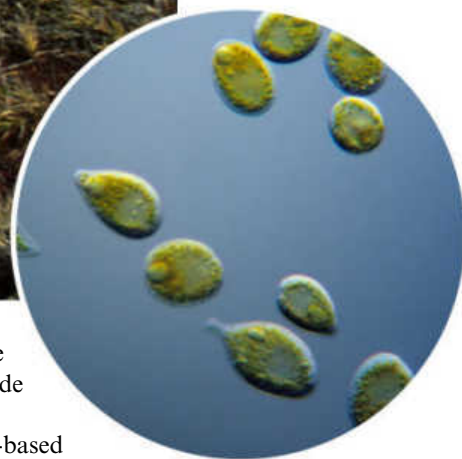
Biochemist George Miljanich — one of the creators of Prialt, the painkiller based on a cone snail toxin — is now seeking a sodium channel blocker from an even more surprising source: saxitoxin, made by bacteria found in the algae that can cause toxic red tides.

Compounds like saxitoxin cause paralytic shellfish poisoning in humans, he says, but these





RED TIDE algal blooms (left) are caused by high concentrations of microscopic plankton (below), several species of which can harbor a potent toxin.



toxins also bind to six out of the nine sodium-channel subtypes. “Our challenge, building on what Mother Nature has given us, is to narrow that selectivity down from the six down to the one, Nav 1.7,” says Miljanich.

Unlike the peptides derived from spider or centipede venoms, saxitoxin is a small molecule, which means any medication based on it can be taken as a pill.

Miljanich believes that a viable alternative to opioids that could work against all pain syndromes could arrive in the next three to four years, most likely as some sort of sodium channel 1.7 blocker. But developing new analgesics is a real challenge. Prialt, he says, was arguably the only new non-opioid analgesic approved by the FDA in the past 20 years.

It’s challenging to find alternatives to opioids because it’s so difficult to craft painkillers without side effects. For instance, the skin toxins of poison-dart frogs drew attention 20 years ago as a potential painkiller that worked by targeting

nicotine receptors. But an effective dose turned out to include toxic side effects.

Researchers working on venom-based painkillers are undeterred. “Mother Nature has been a wonderful, productive source of drugs,” says Miljanich.

And even if engineered components of venom don’t become drugs themselves, they have been useful in pointing out potential new targets, says Olivera, who collaborated with Miljanich in research into conotoxins.

What makes Olivera optimistic in the long run is that venoms offer a tool kit for understanding what happens when you have severe pain. “Basic understanding of what causes pain in the first place is the key to coming up with ways to prevent it,” he says. **D**

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# America's



Arches (left) and Yellowstone (right) national parks, both far from the bright lights of big cities, are prime stargazing sites.





# Outdoor Laboratory

A century ago,  
Congress created the  
**NATIONAL PARK SYSTEM**  
— and ended up  
preserving some of the  
best research sites  
in the world.

BY KRISTIN OHLSON



Ten miles into Death Valley's Johnson Canyon, the recreational hikers had thinned out, but Kelly Iknayan was still on the trail, scouting the grizzled landscape for birds.

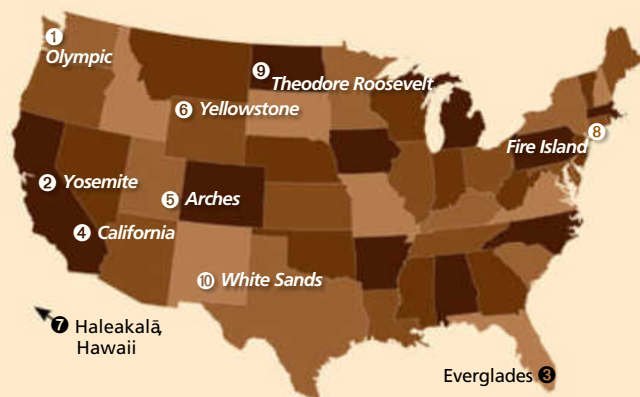
More than 100 years ago, zoologist Joseph Grinnell, the first director of the Museum of Vertebrate Zoology at the University of California, Berkeley, visited this same spot as part of a massive baseline study of California's birds and small mammals. Iknayan, a Berkeley Ph.D. candidate, is following in Grinnell's tracks, surveying birds in Death Valley, Mojave and Joshua Tree national parks as part of a broader 10-year-old effort by UC Berkeley scientists to see how those fauna are faring in the age of climate change.



Kelly Iknayan counts birds in California's Mojave National Preserve.

Iknayan may have been a solitary figure in a remote part of Death Valley that day, but she is hardly the lone scientist working in the United States' 408 national parks. Hundreds don hiking boots, waders or snowshoes every year to conduct research in the parks, from the Florida Everglades to Alaska's Denali.

The National Park System contains some of the most intact landscapes in the world, making it a boon to scientists who study the natural environment. Take geysers, for instance: Half the world's geysers have been destroyed, but geologists can still study them in the protected environment of Yellowstone National Park. The same holds true for many imperiled species, from Yellowstone's bison to Big Bend's Rio Grande silvery minnows, both the subjects of important studies.



Few people would deny the value of national parks now, but these national treasures were hard won. Before the National Park Service's (NPS) official founding in 1916 — 100 years ago in August — there was debate about whether the natural resources in these lands should be managed for economic gain or preserved to provide a necessary respite for the soul, as naturalist John Muir said. At the prodding of Muir and other advocates, Congress chose preservation.

But even the national parks, which enjoy the highest level of protection in the world, are not immune to human impact. In fact, much of what we know about climate change's effects on ecosystems comes from research within park borders.

"Observation of melting glaciers in Glacier National Park and North Cascades National Park has contributed to the global database that tells us glaciers are receding and human climate change is the cause," notes Patrick Gonzalez, NPS's national climate change scientist. Research at other parks investigates a wide range of other environmental threats, including air and noise pollution and invasive species.

Many research projects conducted within the parks aim to help conserve these iconic ecosystems — no easy task, given how much they're changing. "Over the past century, the typical approach to conservation was to try to preserve historical ecological communities, but it's challenging to do that when conditions have changed so much," says Steve Beissinger, a UC Berkeley conservation biologist who helped organize a conference last year on science in the national parks. "We might not be able to keep glaciers in Glacier National Park. Instead, we may have to manage for change based on projected future conditions."

From mountains to seashores, scientists are turning our national parks — called America's "best idea" — into outdoor laboratories, deploying their own best ideas for understanding the natural world and how we affect it. Here, we highlight 10 key research projects underway at parks around the country.





The Elwha River rushes through the gap where Glines Canyon Dam once stood. Just after this photo was taken in 2014, the final piece of the dam was removed.



Game warden Jack Pike shows off his 26-pound catch from the Elwha River in 1915. Salmon this big would become a rarity.

carried away the sediment and deposited most of it in the Strait of Juan de Fuca, the body of water that connects Puget Sound to the Pacific Ocean. Chinooks have been seen in the upper watershed for the first time in 100 years. Research hydrologist Chris Magirl from the U.S. Geological Survey has studied the impact of this huge release of mud: how it changes water flow and turbidity; how the salmon use the sediment to build nests; and how quickly the water clears up.

The benefits of what he's learning on the Elwha ripple beyond the park. Magirl was called in to consult on the fatal mudslide in Oso, Wash., in 2014 to make sure a second landslide didn't bury the 1,000 rescuers who rushed to the site. "Many of the scientific tools we used on the Elwha about massive releases of sediment were applied to Oso," Magirl says.



In this 2014 photo, a newly freed Elwha River carries sediment into the Strait of Juan de Fuca.



## Olympic National Park, Washington

### Can Removing a Dam Resurrect a River?

One hundred years ago, the Elwha River, which flows through Olympic National Park, was a sort of paradise for salmon, especially chinook. Back then, they reputedly weighed up to 100 pounds. But when an entrepreneur named Thomas Aldwell built a dam for hydroelectric power without the fish ladders that allow salmon to surmount

the dam — even though state regulations required them — most of the fish were cut off from their spawning grounds upstream. At the same time, sediment that would have flowed downstream and formed sandbars and eddies built up behind the dam, completed in 1913, and another constructed later. The entire riverine ecosystem suffered.

In 1992, at the behest of scientists and conservationists, Congress passed a law to restore the Elwha River. The park service decided to remove both dams over three years to free the river — and the 21 million cubic meters of sediment that had built up behind them. Park officials set off the final explosion in 2014.

As they hoped, the river





## Yosemite National Park, California

### Forests Altered by Fire

A century ago, visitors to the West's forests trod a mosaic of sun and shadow, navigating stands of large trees and open spaces. Today, a walk in the woods is a dimmer experience. Many forests are crowded with trees, and branches obscure the sky. This new denser forest structure is an artifact of 82 years of snuffing out fires across the region.

Before the age of fire

suppression, wildfires regularly moved through forests — every few years in some, every few decades in others — keeping new growth in check. The result was often a clumpy forest structure with thick stands of large trees separated by open spaces, which forest scientists later learned tends to slow down the speed and intensity of future fires. Today's forest managers are trying to return

forests to some semblance of their historic open structure by removing trees that have sprouted up in the absence of fire, through mechanical thinning or controlled burns. Those open spaces serve as natural firebreaks, helping to prevent high-intensity fires.

Toward this goal, Van Kane from the Forest Structure and Dynamics Lab at the University of Washington's School of

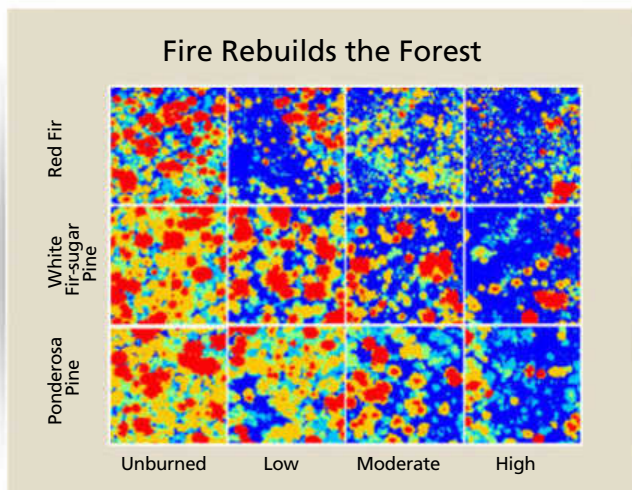
Environmental and Forest Sciences is studying how fire has changed forest structure in Yosemite National Park. Kane uses a remote sensing tool called LIDAR, which beams laser pulses over the landscape from a plane. The reflection from these pulses — off treetops, foliage and branches, all the way to the ground — reveals both the vertical and horizontal array of vegetation below.

With this information, Kane can assess forest patterns before and after fires over much larger areas than previously possible. His research shows that all fires are not the same: Severe, superhot fires will kill many trees, but low- and moderate-severity fires can return the forest to a healthy state.

"We're showing that if you let the moderate fires burn, they will do a good job of restructuring forests and making them overall more fireproof," Kane says. "We have data over tens of thousands more acres than previously, and we can really look at the patterns and build up statistics." Kane says the work is helping forest managers improve fire management strategies.



Land managers use prescribed fire, like this 2003 burn in Yosemite, to keep overgrowth at bay.



LIDAR data from Yosemite provide a colorful picture of how fire intensity affects forest structure in different forest types. Researcher Van Kane found that as intensity increased, the canopy (red and orange) decreased, while the number of gaps (blue) increased, creating a mosaic of openings and forest stands in low- to moderately burned areas.



Wildfires like the 2014 El Portal fire in Yosemite can alter forest structure.





Scientists have breached this levee to allow water to move between the basins it divides. They track the flows with fluorescent dye.



Historical flow



Current flow



Restored flow

### A Wetland Divided

Historically, water in the Everglades flowed freely across much of South Florida (top). Urban development, agriculture and levees have shrunk and diverted the “river of grass” (center), but scientists hope to restore a large swath of it (bottom).



## Everglades National Park, Florida

Restoring the ‘River of Grass’

Florida’s Everglades — the “river of grass” — once covered nearly 4,200 square miles. Humans began to constrict and alter this incredibly rich ecosystem in the early 1900s, when parts were drained for agriculture and urban development. In recent decades, people have come to recognize the many benefits of this vast sheet of wetlands, 100 miles long and 40 miles wide, which provides water to 7 million people.

Congress has mandated the

restoration of the Everglades, but it’s unclear how to bring back enough of the system’s natural flow to return the ecosystem to health. U.S. Geological Survey hydrologist Jud Harvey and colleagues are studying the impact of restored flow in a 2-square-mile section of the Everglades where a levee has been breached. In 2014 and 2015, Harvey and his team boosted flows from November to January each year. The hope is that these pulses of water will pick up organic



Scientist Corey Whittaker takes measurements during an experimental high flow in the Everglades.

sediment particles from sloughs and deposit them on ridges, restoring the patterns that supported diverse flora and fauna in the past.

“It’s been exciting to open the floodgates,” Harvey says. “We can’t restore the Everglades to pre-Columbian times, but we’ll be able to make some decisions about how much flow we need for a big increase in benefits.” Harvey’s work has implications for stream and wetland restoration around the world.





## California national parks

### How Has Climate Change Altered the Distribution of Native Animals?

In 1908, biologist Joseph Grinnell began conducting a survey of birds and small mammals in the West and tracked their distribution and ecological niches. At the time, he said the value of this work — conducted for the Museum of Vertebrate Zoology at UC Berkeley, where he was director — would not be appreciated for a century, assuming the materials were preserved for students of the future.

Today, Berkeley conservation biologist Steven Beissinger well appreciates the value of those

surveys. “We are those students of the future!” he says. He and his colleagues use Grinnell’s data to understand how climate change has affected the distribution of these species.

So far, after conducting studies in Yosemite, Sequoia, King’s Canyon and Lassen Volcanic national parks, they’ve found a perplexing jumble of migrations. While the team observed some consistent upward shifts in range to cooler areas, they also found that some species didn’t move, and that others even migrated

downslope. “Climate change is lumpy,” says Beissinger, who is also studying more arid sites such as Death Valley, Mojave and Joshua Tree. “We still don’t see a simple way to predict what some of the effects of it will be.”

Once Beissinger and his team better understand which species are moving and why, park managers may be able to help species survive by removing barriers to their dispersal to different elevations or by relocating them to more suitable habitats.



*Joseph Grinnell’s early species surveys are being used today to assess climate change impacts.*



Mojave National Preserve





## Arches National Park, Utah

Testing the Strength of Fragile Geologic Structures



Researcher Alison Starr, a member of Jeffrey Moore's team, sets up a seismometer on Surprise Arch to discover its vibrational signature.

Few images are as iconic as the soaring sandstone spans in Arches National Park. But should we be walking under them? Are they safe? Not always. In 2008, the 12th largest of the park's 2,000 arches, Wall Arch, tumbled to the ground during the night.

Geologist Jeffrey Moore has figured out a way to study the viability of the arches with engineering tools designed to test airplane wings and bridges. "Until now, there has been no method available to sense damage or decaying strength in such structures without invasive monitoring," he says.

Moore measures how the arches vibrate to the background shaking of the Earth caused by natural processes like wind and distant ocean tides to arrive at a vibrational signature for each arch. With this baseline established, scientists can determine whether a recent



Wall Arch before and after its collapse. New research aims to help park officials gauge arch sturdiness.

event — an earthquake or a new fracking operation, for instance — has changed the arch's vibrational characteristics and, consequently, its mechanical composition. The arches are like geologic harp strings, always moving and responding to events near and far, but scientists are now close to creating a better tool for understanding when one might snap.



## Yellowstone National Park, Wyoming

Exploring the Geothermal Piping of a Supervolcano

Park visitors gather around Yellowstone's Old Faithful geyser expecting a 145-foot gush of boiling water and steam every 90 minutes. It's a display as seemingly predictable as the park's live animal shows or nature walks. But scientists have long wondered why geysers spout instead of trickle, like a hot spring.

Studies by UC Berkeley's Michael Manga of the park's Lone Star geyser and the El Hefe geyser in Chile suggest a complex plumbing system allows steam to accumulate in a series of traps. The steam heats the water column, which begins to boil from the top, then below, leading to a thunderous explosion.

The University of Utah's Hsin-Hua Huang has solved another mystery from Yellowstone, the site of one of the world's largest supervolcanoes. Beneath a known magma reservoir below the park, Huang's team recently discovered a much larger reservoir of magma 12 to 31 miles underground. Based on the volume of carbon dioxide venting from the earth, scientists suspected this second pit of hot, partly molten rock existed, but it had never been located.

Huang's work fills in some of the blank space between the shallower chamber and the hotspot plume, which starts at about 40 miles down and extends into the mantle.

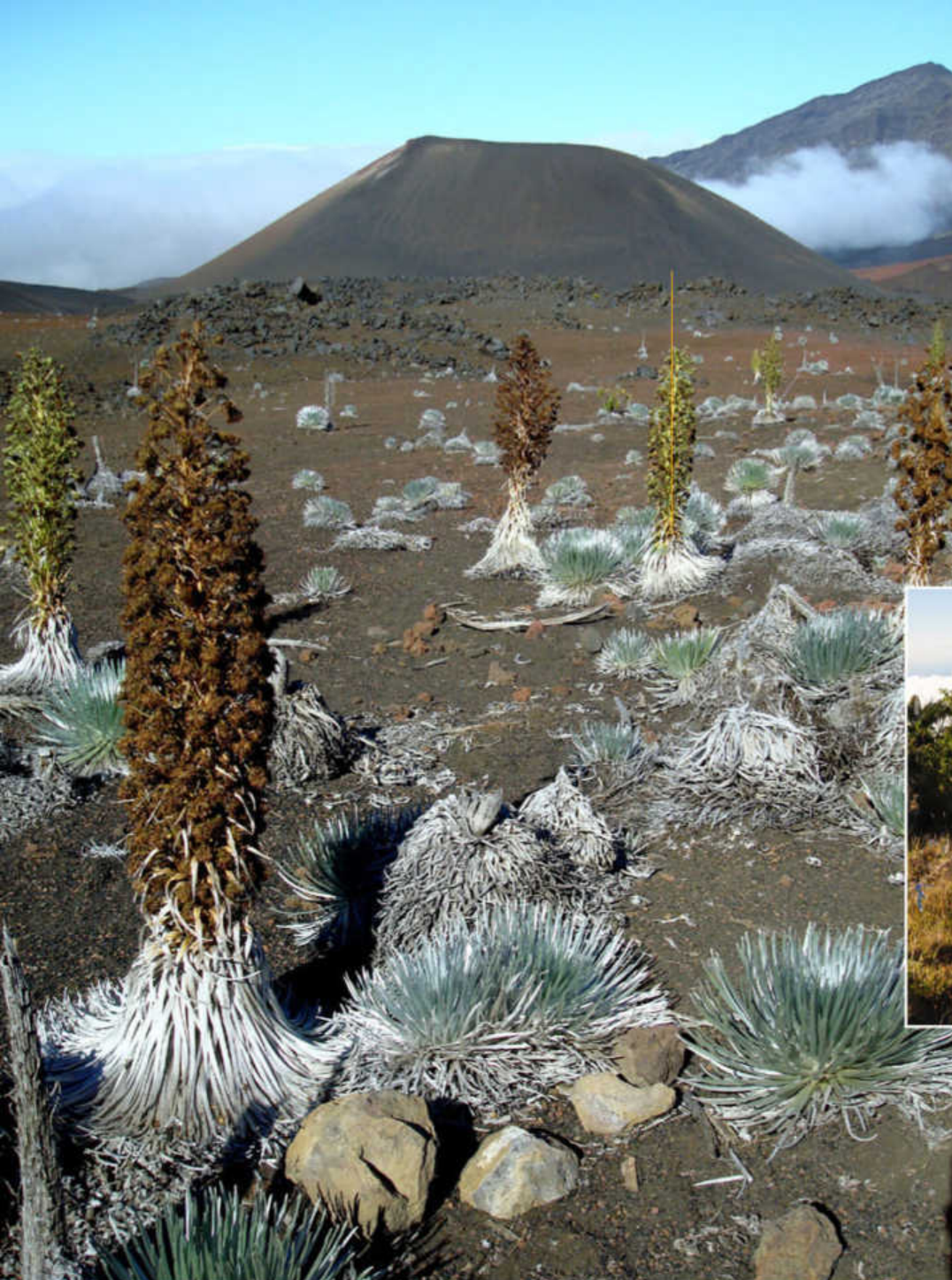


Yellowstone's Lone Star geyser

He surmises that magma rises from the plume and pools in the lower chamber, a kind of waiting room, before moving to the upper chamber. The discovery of the new

reservoir will help geologists understand how these major volcano systems work and, perhaps, provide a way to more accurately assess hazards in the future.





The Haleakalā silversword (left) is one of several rare alpine species that could lose out as the cloud forests in its namesake park creep higher. Ecologist Shelley Crausbay (below, checking a climate monitor) is studying how the drying effect of El Niño influences ecosystem dynamics in the park.



other rare species, including the silversword, a spiky plant that can live up to 90 years, blooming once before it dies. Much as gardeners can distinguish a rose from a daisy just by looking at the flower, scientists can distinguish what kind of plants used to live in a certain landscape by looking at fossilized pollen. By comparing the pollen records at different elevations with paleoclimate records, Crausbay has concluded that El Niño-driven droughts determine the upper limits of the forest.

"Looking at this older material allows us to get a deeper baseline on some of these ecological phenomena that can play out over thousands of years," Crausbay says. "You can only get a glimmer of that by looking solely at the modern landscape."



## Haleakalā National Park, Hawaii

### How Does El Niño Affect Tropical Cloud Forests?

Predicting the impact of climate change on ecological communities is tricky, but predicting the impact of El Niño, the cyclical warming in the Pacific Ocean that affects temperature and rainfall around the globe, is even trickier. El Niño patterns are a strong driver of drought in

Hawaii, and Haleakalā National Park offers researchers a great opportunity to study the patterns' impact on ecosystems in the region.

A team led by University of California, Santa Barbara plant ecologist Shelley Crausbay is studying high-elevation cloud forests that provide habitat

for a number of rare birds, most of which are endangered. The forests have climbed up and down the mountains over millennia.

When the forests move upward, they offer more habitat for the birds but squeeze the alpine ecosystem that supports a number of





## Fire Island National Seashore, New York

Gauging Coastal Ecosystems' Resiliency to Extreme Storms



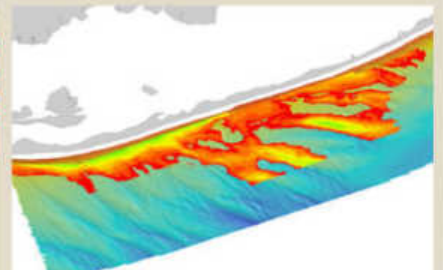
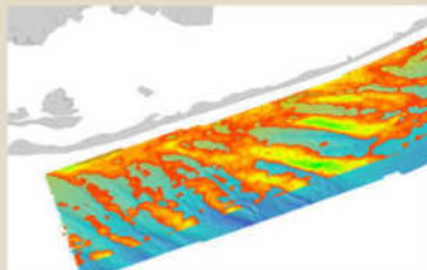
Superstorm Sandy in 2012 was a disaster for the places where humans live, but not for natural coastal ecosystems. That's the conclusion of NPS ecologist Mary Foley, whose team is studying the response of natural ecosystems in Fire Island National Seashore in New York and in Assateague Island National Seashore in Maryland and Virginia, Gateway National Recreation Area in New York City and New Jersey, and others.

"Sand was moved around and altered, but the ecosystems were not damaged by this

enormous hurricane," Foley notes. Some of the 30 studies suggest features of coastal ecosystems may even protect the built environment during a natural disaster. In particular, Foley points to the ridges of sand perpendicular to the shoreline at Fire Island. While cities and the Army Corps of Engineers sometimes mine them to shore up eroding beaches, they may want to reconsider: Those sandbars might slow down hurricanes, reducing the damage to communities along the shoreline.



### Shifting Sands



Left: NPS researchers measure sand depth. Right: Maps show the extent and thickness of sand ridges along the ocean-facing side of Fire Island in 1996 (middle) and in 2014 (right), after Superstorm Sandy tore through the area. Thicker areas are in green; thinnest areas are in red.



## Theodore Roosevelt National Park, North Dakota

### Tracking Oil and Gas Development's Effect on Air Quality

Hikers and campers heading into the backcountry of Theodore Roosevelt National Park tip their heads back when the sun goes down, expecting a brilliant display of stars set against a dark sky. But what they often see in the distance are gas flares and the lights of drilling rigs, bleaching the sky so that it's hard to make out the stars. In the daytime, especially when the winds are low, they sometimes strain to see natural vistas through a scrim of haze.

Roosevelt, which lies in the heart of the Bakken shale formation, is surrounded by oil and gas development. North Dakota alone is home to about 10,000 active wells that together produce more than

1 million barrels of oil each day, and the number of wells is expected to grow to up to 60,000 over the next 25 years.

Extracting oil also releases natural gas from the formations, but since North Dakota doesn't have the infrastructure to pipe it away, about one-quarter of the gas is burned on site, or "flared off." NPS chemist Tony Prenni and colleagues are studying the impact of all that petrochemical activity on visibility in Roosevelt and other parks in the region. Because of Clean Air Act regulations, visibility has steadily improved around the country in recent decades, but it remains a problem in this area.

"The good news is that

the emissions are not at the point where they're a health concern," Prenni says. "Still, you don't expect to go into a national park and find poor air quality. And night skies are considered a resource in the park." Prenni is gathering

better measurements and conducting particle analyses that will help park managers assess this threat, not just at Theodore Roosevelt but also at other parks in the West surrounded by oil and gas development.



The park's nighttime view now includes the glow of an oil field.



In this spacecraft view of the U.S., the luminosity of North Dakota's Bakken oil field rivals that of even the largest cities.



A pumpjack plumbs the Bakken oil field against a backdrop of gas flares.

FROM TOP: JEFF ZYLLAND/NATIONAL PARK SERVICE; NASA EARTH OBSERVATORY/NOAA; NGDC; GREG LATZA





Researcher Erica Bree Rosenblum examines a lesser earless lizard at White Sands National Monument.



Top: These lizards are the same species, but one has adapted to the park's whiteout conditions. Left: A hiker takes in the dunes.

White Sands lizards are on their way to becoming separate species, with longer limbs and brain structures different from their darker neighbors.

"We've been able to identify some of the genetic mechanisms for the changes we see," Rosenblum says. "For most species, we know almost nothing about the specific genes involved in speciation, and White Sands is one of the few places where we can link together all the pieces of the puzzle. It's an incredibly cool place to study evolution in action — very different from looking back millions of years at dinosaurs." Her work is contributing to scientists' understanding of evolution and also provides material for an exhibit in the park. **D**

**Kristin Ohlson** is a freelance writer based in Portland, Ore.



## White Sands National Monument, New Mexico

### How Quickly Can New Species Evolve?

The alabaster dunes at White Sands National Monument are a geologically recent phenomenon, formed only a few thousand years ago and still changing. Many of the creatures in the White Sands ecosystem, including the lesser earless lizard and the

Apache pocket mouse, have undergone rapid evolution in response to their unique environment, developing a lighter appearance that allows them to blend into the gypsum sands and escape predators.

Berkeley evolutionary biologist Erica Bree Rosenblum

is studying this phenomenon in multiple species, including lizards, invertebrates and mammals, comparing them with their brown relatives in the adjacent desert and tracking changes in everything from genes to mating patterns. So far, she has found that the



# Germ of an IDEA

In the 1890s, **WILLIAM COLEY** figured out a way to destroy cancerous tumors by injecting patients with toxic bacteria. Debunked at the time, his treatments laid the groundwork for modern immunotherapy.

BY **CARL ENGELKING**

In 1891, a man could plunge a syringe loaded with toxic bacteria into the neck of another man — simply on a hunch.

In May of that year, William B. Coley was the man holding that dubious syringe in the apartment of a 35-year-old Italian immigrant and drug addict named Zola. Poor Zola was told he might have only weeks to live due to an egg-size, inoperable tumor obstructing his pharynx, making it impossible for him to swallow food. Zola's last shot at survival was in the hands of Coley, a 29-year-old bone surgeon who had just completed his training at New York Memorial Hospital. The young surgeon believed he was holding a cure for cancer in that syringe.

Coley was fascinated by a smattering of curious cancer stories referenced in the medical literature of the era: Patients riddled with inoperable tumors suddenly found themselves cancer-free after contracting erysipelas, another potentially fatal ailment at the time, caused by *Streptococcus* bacteria and marked by fever and hardened, painful rashes. Coley unearthed 47 similar cases and grew so intrigued by the apparent link that he scoured the ghettos of New York's Lower East Side to find a German immigrant whose cancer had disappeared, according to medical records, after contracting erysipelas following several failed attempts to remove his tumor. Coley eventually found his man, scars and all, who was free of disease and in good health — seven years after doctors considered his case hopeless.

That was all Coley needed to proceed directly to human trials, and Zola would become his first test subject. Coley filled a syringe with living *Streptococcus pyogenes*, known to induce erysipelas attacks, and injected the solution directly into Zola's tumor. It took awhile — in fact, it took repeated injections over five months — but finally, an hour after one particular injection in October, Zola broke out into sweaty chills, and his body temperature soared to 105 degrees.

Just two days into the throes of erysipelas, the man's tumor began to liquefy and shrink; within two weeks, it completely disappeared. Zola's immune system had turned its weaponry against the tumor after a call to action from a feverish infection. According to follow-up reports, Zola remained well for eight more years before dying from a recurrence of the tumor in his native Italy.

Coley wasn't the first to observe this compelling quirk of the immune system that gave Zola and others extra years on their lives, if not complete remission. The earliest mention of cancer-fighting infections dates to a citation from 1550 B.C. and is attributed to Egyptian physician Imhotep, who called for treating the wound with cloth coated in a poultice that would almost certainly lead to infection, and then cutting into the tumor. Coley, however, was the first to study and test the efficacy of what would come to be known as immunotherapy, coaxing the human immune system to fight cancer.

After his success with Zola in that New York apartment, Coley dedicated the next 40 years of his life to



perfecting his unorthodox cancer treatment. In the process, he would become both a nationally revered cancer surgeon and an embattled figure who stubbornly defended both his treatment and his reputation until his death in 1936. Now, more than 100 years after his first fateful success, cancer researchers are still traveling the path Coley blazed long ago.

## RISE AND FALL

In the two years following Zola's treatment, Coley treated 10 more patients with live bacteria, but his approach proved to be highly unpredictable. Sometimes he couldn't induce an infection; other times, patients had strong reactions but saw no cancer-fighting effect. On two consecutive occasions, the erysipelas infection killed the patients. So Coley changed course and crafted a vaccine with two dead bacteria, *S. pyogenes* and *Serratia marcescens*. Research at the time indicated the latter increased the virulence of the former when combined with each other, allowing the injections to induce the feverish effects while drastically reducing the risk of death. This reimagined mixture became known as Coley's Toxin.

The pharmaceutical firm Parke-Davis & Co. made various formulations of Coley's Toxin available to all physicians from 1899 to 1951, and at least 42 physicians from Europe and North America reported success stories in patients treated with the toxin, specifically for bone and soft-tissue sarcomas. In a 1945 study of the toxins' efficacy, among 312 inoperable cases of cancer, 190 were considered regressions after treatment — a cure rate of about 60 percent. Coley went on to treat nearly 1,000 patients with his toxin and published more than 150 papers on the subject.

The widespread use of his treatment and his prolific publishing record made Coley a leading cancer expert in the eyes of the public. And Coley was justly regarded for his success as a cancer surgeon — he retired from New York Memorial Hospital in 1933 as chief of the bone tumor service. (His son Bradley was appointed his successor.) In 1935 Coley was inducted as an honorary fellow into the Royal College of Surgeons of England, becoming just the fifth American to receive that honor. But where his toxin was concerned, Coley was a target for criticism in the medical community, and with good reason: His breakthrough was built upon a shaky foundation.

Coley may have been an audacious clinician whose work helped hundreds of patients, but a scientist, he was not. He knew how to treat his patients, but he was never trained in laboratory work, and his toxin research didn't meet the increasingly stringent scientific standards of the era. Physicians chided Coley for poorly controlled and documented experiments. For example, he injected the toxin into multiple locations in test patients without properly noting the location of each injection.

Despite his best efforts, the toxin was still inconsistent at best: Thirteen different formulations of his toxin were produced at one point, with some mixtures more effective than others. Furthermore, each patient reacted unpredictably to



William Coley, now regarded as the father of immunology, did not earn that moniker so easily.

the toxins, and the toxins still were sometimes fatal.

But even if Coley had been more meticulous, he was still battling a medical establishment that firmly believed any cancer cure that didn't require surgery meant the "disease" was misdiagnosed as cancer. Plus, many doctors had a justifiably hard time reconciling the Hippocratic oath with the idea of inducing a potentially fatal infection in already-suffering patients.

Early in the 20th century, radiation therapy was also an emerging cancer treatment, and the nation's preeminent cancer pathologist, James Ewing, staunchly favored treating patients with this promising new method. Ewing also happened to be Coley's boss and biggest opponent — never a good combination. Ewing forbade Coley from using his toxin inside Memorial Hospital.

Coley's research had one major, damning flaw: He couldn't explain why his toxins worked. They just did (sometimes). Until the day he died, Coley tenaciously held to the belief that microorganisms caused cancer — a theory long dismissed by the medical establishment — and that his toxin somehow killed those cancer-causing organisms in the body.

He must not have been alone in this conviction. More than 15 years after Coley's death — not of cancer, incidentally, or an ironic erysipelas infection, but of chronic diverticulitis — Parke-Davis continued to make Coley's Toxin, even as chemotherapy and radiation rose to the forefront of cancer treatment. By 1962, however, the U.S. Food and Drug Administration refused to acknowledge the toxin as a proven drug and made it illegal to use to treat cancer. Still, the legacy of Coley's Toxin would not be forgotten.

## COLEY VINDICATED

Over the next several decades, researchers stuck their toes into the murky and temperamental waters of immunotherapy. Since the 1960s, the medical community has gone back and forth as to whether the immune system could be made to launch an anti-tumor offensive. It's only relatively recently that researchers have finally confirmed that, yes, our immune system is indeed programmed to fight cancer.

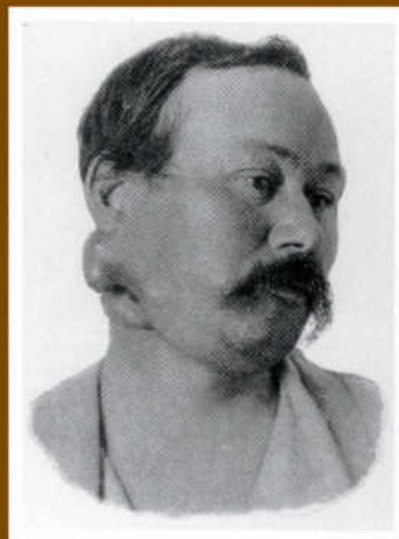
Coley's daughter, Helen Coley Nauts, deserves a lot of credit for keeping her father's legacy relevant. After her father died, she dedicated her life to studying his toxins and reviewing his work. Although Nauts herself had no formal medical training, she published more than 18 monographs and identified more than 500 patients who were successfully treated with her father's toxin. In 1953, she founded the Cancer Research Institute, which still exists today, to honor her father and advance the field of immunotherapy research. Up to the end of her life in 2001, Nauts was tireless — some might even say obsessed — in her efforts to have her father's work reappraised by mainstream cancer researchers.

She largely succeeded. Today, immunotherapy is a rapidly ascending field of cancer research because scientists are finally figuring out the immune system's quirks, and the pharmaceutical industry is getting into the game. "Immunotherapy is probably the hottest area of cancer research right now," says Jill O'Donnell-Tormey, CEO and director of scientific affairs at the Cancer Research Institute. She notes

that biotech firms are investing heavily in immunotherapy research, and about 40 percent of the roughly 6,000 cancer clinical trials taking place in the United States today include some form of immunotherapy.

"I've been [at the Cancer Research Institute] for 28 years, and I have never seen the excitement in the field like this," O'Donnell-Tormey says. "In the last few years, it's all come together. Scientific understanding has helped build a rational case of how this works, and now we can couple that with clinical results."

The momentum started building in 2010 when the FDA approved Provenge, a cancer vaccine that rallies male patients' immune systems to attack prostate cancer cells, allowing patients with an advanced form of the cancer to live several



For Zola (left), Coley's toxin-triggered infection liquefied the tumor in days. But toxin-induced infections were unpredictable. The patient at right had 63 injections before his tumor shrank. Some patients died.

months longer. Provenge proved to researchers that it is possible to get an active immunotherapy approved by the FDA.

The next year, the FDA approved another immunotherapy agent, ipilimumab, to treat melanoma. The drug blocks CTLA-4, a protein receptor on the surface of T-cells that serves as a molecular stop sign, preventing the immune system from going into overdrive. Ipilimumab counters the CTLA-4 signal, allowing T-cells to launch a full-scale attack on cancer cells.

"That's when Big Pharma started sniffing around and really got interested in immunotherapy," says Jeffrey Schlom, chief of the National Cancer Institute's Laboratory of Tumor Immunology and Biology.

BioMed Valley Discoveries in Kansas City is one of those pharmaceutical companies hot on the immunotherapy trail. One of BioMed's projects involves an unorthodox way to penetrate cancer's armor, and the team's approach would no doubt make Coley smile. The BioMed team successfully treated rats, dogs and one human by injecting tumors with a weakened version of *Clostridium novyi*, a toxic bacterium that lives in the soil. Like Coley's initial bacteria of choice, *C. novyi* also



has a dark side: It can cause flesh-ravaging, potentially fatal infections in its natural state. But the researchers' version of *C. novyi* was stripped of its ability to produce a particular toxin. Injecting spores of *C. novyi* into dogs resulted in rapid reduction of tumor sizes, and even completely eradicated tumors in three of 16 trial dogs. When the team injected the first human with the bacteria, it was as if researchers had traveled back in time to Zola's New York apartment.

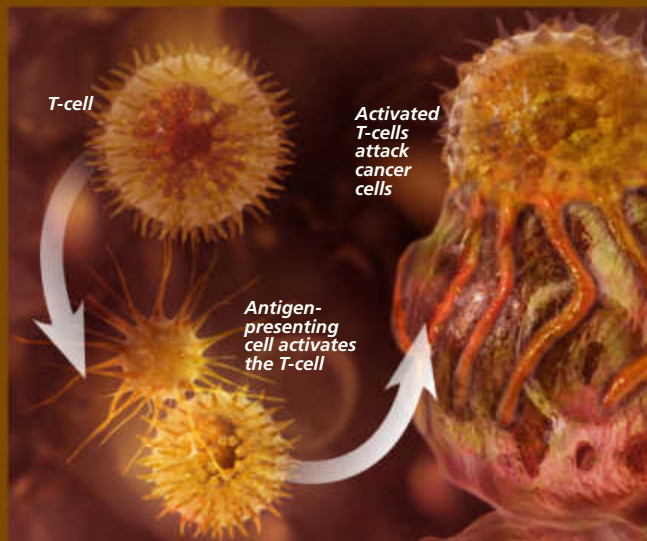
"Coley injected his first patient a century ago, and what he saw was almost identical to what we saw in our first patient," says Saurabh Saha, a partner with Atlas Venture, former BioMed Valley researcher and senior author of the study. "Within the same time frame observed by Coley, our patient developed a fever, the tumor started swelling, and

Researchers are also experimenting with another form of immunotherapy called adoptive cell transfer, which harvests and then reintroduces patients' tumor-infiltrating lymphocytes — cells with anti-tumor capabilities that dig deep behind enemy lines. The idea is that these cells may be present in the body, but their population isn't large enough to exert an anti-tumor effect. So scientists choose the lymphocytes with the greatest tumor-fighting activity, grow a large population of them in the lab, then infuse them back into the patient.

Schlom, of the National Cancer Institute, says the next challenge for researchers is to find ways to combine different immunotherapy drugs into single treatments and measure their efficacy in clinical trials. He says different immune system-enhancing drugs, when combined, can result in better



Coley (left photo, middle, at age 30) spent years butting heads with the medical establishment — including his boss — to accept his toxins. His daughter, Helen Coley Nauts (right), kept up the fight.



Although Coley couldn't explain precisely why or how his toxins worked, modern immunotherapy treatments help T-cells in the immune system to recognize specific cancer cells and attack them.

then it started to shrink."

*C. novyi* is really a two-pronged weapon against cancer: It germinates in tumors and releases cancer-killing enzymes, and it may also trigger an immune response similar to Coley's Toxin. Since *C. novyi* survives only in oxygen-poor environments — tumors can be notoriously void of oxygen — the bacteria die when they reach healthy, oxygen-rich tissues, sparing collateral damage. Essentially, the injections perform highly precise biosurgery from the inside out.

## IMMUNOTHERAPY'S RESURGENCE

BioMed Valley's intriguing *C. novyi* treatment is still in its early stages of testing and research, and it's just one of many ascending immunotherapy treatments. In December 2014 the FDA approved Opdivo (nivolumab), which, like ipilimumab, is another checkpoint inhibitor to treat melanoma. (Opdivo just applies the brakes in a different way.) As a follow-up act, the FDA in September 2015 gave the green light to the first cancer therapy to combine nivolumab and ipilimumab to treat certain patients with metastatic melanoma.

anti-tumor effects. The same rings true when immunotherapy is paired with other cancer treatments like chemotherapy, for example. But testing new combinations presents an entirely different problem. "A lot of these drugs are being made by different companies, and getting them to work together will be difficult," says Schlom.

More than a hundred years after that fateful day in 1891, Coley's legacy may be more relevant than ever. Today's immunotherapy researchers not only will need to borrow the methods once popularized by Coley, but also his implacable personality. But the tide is certainly turning, and persistence is paying off.

"I most admire Coley's tenacity and stubbornness. He kept moving forward with what he thought was an effective means to destroy cancer, despite his colleagues' lack of support," says Saha. "It's unfortunate he was once pushed to the background, but the field has been resurrected 100 years later." **D**

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Do  
winning  
players  
rely  
more on  
**skill,**  
or do they  
just get  
**lucky?**

# Game On

BY ADAM KUCHARSKI

ILLUSTRATIONS BY JOHN DEVOLLE/IKON IMAGES/CORBIS







**I**F YOU EVER VISIT A LAS VEGAS CASINO, LOOK UP. Hundreds of cameras cling to the ceiling like jet-black barnacles, watching the tables below. The artificial eyes are there to protect the casino's income from the quick-witted and light-fingered. Until the 1960s, casinos' definition of such cheating was fairly clear-cut. They only had to worry about things like dealers paying out on losing hands or players slipping high-value chips into their stake after the roulette ball had landed. The games themselves were fine; they were unbeatable.

Except it turned out that wasn't true.

Mathematics professor Edward Thorp found a loophole in blackjack big enough to fit a best-selling book through. Then a group of physics students tamed roulette, traditionally the epitome of chance. Beyond the casino floor, people even scooped lottery jackpots using a mix of math and manpower.

The debate over whether winning depends on luck or skill is now spreading to other games. It may even determine the fate of the once lucrative American poker industry. In 2011, U.S. authorities shut down a number of major poker websites, bringing an end to the "poker boom" that had gripped the country for the previous few years. The legislative muscle for the shake-up came from the Unlawful Internet Gambling Enforcement Act. Passed in 2006, it banned bank transfers related to betting when the "opportunity to win is predominantly subject to chance." Although the act has helped curb the spread of poker, it doesn't cover stock trading or horse racing. So how do we decide what makes something a game of chance?

## POKER FACES

The answer turned out to be worth a lot to one man. As well as taking on the big poker companies, federal authorities had gone after people operating smaller games. That included Lawrence DiCristina, who ran a poker room on Staten Island in New York. The case went to trial in 2012, and DiCristina was convicted of operating an illegal gambling business.

DiCristina launched a motion to dismiss the conviction, and the following month, he was back in court arguing his case. During the hearing, DiCristina's lawyer called economist Randal Heeb as an expert witness. Heeb's aim was to convince the judge that poker was predominantly a game of skill and didn't fall under the definition of illegal gambling. He presented data

from millions of online poker games and showed that, bar a few bad days, top-ranked players won pretty consistently. In contrast, the worst players lost throughout the year. The fact that some people could make a living from poker was surely evidence that the game involved skill.

The prosecution also had an expert witness, an economist named David DeRosa. He didn't share Heeb's views about poker. DeRosa used a computer to simulate what might happen if 1,000 people each tossed a coin 10,000 times, assuming a certain outcome — such as tails — was equivalent to a win and the number of times a particular person won the toss was random. But the results were remarkably similar to those Heeb presented: A handful of people appeared to win consistently, and another group seemed to lose a large number of times. This wasn't evidence that a coin toss involved skill, just that — much like the infinite number of monkeys typing — unlikely events can happen if we look at

a large enough group.

Another concern for DeRosa was the number of players who lost money. Based on Heeb's data, about 95 percent of people playing online poker ended up out of pocket. "How could it be skillful playing if you're losing money?" DeRosa asked.

Heeb admitted, in a particular game, only 10 to 20 percent of players were skillful enough to win consistently. He said the reason so many more people lost than won was partly down to the house fee, with poker operators taking a cut from the pot in each round. But he didn't think the apparent existence of a poker elite was due to chance. Although a small group may appear to win consistently if lots of people flip coins, good poker players generally continue to win after they've ranked highly. The same cannot be said for the people

How do  
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who are fortunate with coin tosses.

According to Heeb, part of the reason players can win is that in poker, players have control over events. If bettors bet on a sports match or a roulette wheel, their wagers don't affect the result. But poker players can change the outcome of games with their betting. "In poker, the wager is not in the same sense a wager on the outcome," Heeb said. "It is the strategic choice that you are making. You are trying to influence the outcome of the game."

But DeRosa argued that it doesn't make sense to look at a player's performance over several hands. The cards dealt are different each time, so each hand is independent of the last. If one hand involves a lot of luck, there's no reason to think that player will have a successful round after a costly one. DeRosa compared the situation to the Monte Carlo fallacy. "If red has come up 20 times in a row in roulette," he said, "it does not mean that 'black is due.'"

Heeb conceded that a single hand involves a lot of chance, but it didn't mean the game was chiefly one of luck. He used the example of the baseball pitcher. Although pitching involves skill, a pitch is also susceptible to chance: A weak pitcher could throw a good ball, and a strong pitcher a bad one. To identify the best — and worst — pitchers, we need to look at many throws.

The key issue, Heeb argued, is how long it takes for the effects to outweigh chance. If it takes a large number of hands (that is, longer than most people will play), then poker should be viewed as a game of chance. Heeb's analysis of the online poker games suggested this wasn't the case. It seemed that skill overtook luck after a relatively small number of hands. After a few sessions of play, a skillful player could therefore expect to hold an advantage.

It fell to the judge, a New Yorker named Jack Weinstein, to weigh the arguments. Weinstein noted the law used to convict DiCristina — the Illegal Gambling Business Act — listed games like roulette and slot machines but didn't explicitly mention poker. Though Weinstein said this didn't automatically mean the game wasn't gambling, the omission meant the role of chance in poker was up for debate. And Weinstein had found Heeb's evidence convincing. On Aug. 21, 2012, he ruled that poker was predominantly governed by skill rather than chance and did not count as gambling under federal law. DiCristina's conviction was overturned.

The victory was short-lived, however. Although Weinstein ruled DiCristina hadn't broken federal law, the state of New York has a stricter definition of gambling. Its laws cover any game that "depends in a material way upon an element of chance." As a result, the state law meant poker

still fell under the definition of a gambling business.

The DiCristina case is part of a growing debate about how much luck comes into play in games like poker. Definitions like "material degree of chance" will undoubtedly raise more questions. Given the close links between gambling and certain parts of finance, surely this definition would cover some financial investments, too? Where do we draw the line between flair and fluke?

## LUCK OR SKILL?

It's tempting to sort games into separate boxes marked "luck" and "skill." Roulette, often an example of pure luck, might go into one. Chess, a game many believe relies only on skill, might go in the other. But it isn't this simple. To start with, processes we think are as good as random are usually far from it.

Despite its popular image as the epitome of randomness,



The 2012 federal trial of poker club operator Lawrence DiCristina (above), with economists Randal Heeb (top) and David DeRosa (bottom) as expert witnesses, added to the growing debate of whether poker requires skill or falls to chance.



roulette was first beaten with statistics, and then with physics. Other games have fallen to the scientific method, too. Card counters have made blackjack profitable, and syndicates have turned lotteries into investments.

Moreover, games that we assume rely solely on skill do not. Take chess. There's no inherent randomness in a game of chess: If two players make identical moves every time, the result will always be the same. But luck still plays a role. Because the optimal strategy isn't known, there's a chance a series of random moves could defeat even the best player.

Unfortunately, when it comes to making decisions, we sometimes take a rather one-sided view of chance. If our choices do well, we put it down to skill; if they fail, it's bad luck. External sources can also skew our notion of skill. Newspapers print stories about entrepreneurs who hit a trend and make millions, or celebrities who suddenly become household names. We hear tales of new writers who pen instant best-sellers and bands

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that become famous overnight. We see success and wonder why those people are so special. But what if they're not?

In 2006, Matthew Salganik and his colleagues at Columbia University published a study of an artificial "music market," in which participants could listen to, rate and download dozens of different tracks. In total, there were 14,000 participants, whom the researchers secretly split into nine groups. In eight of the groups, participants could see which tracks were popular with their fellow group members. The final group was the control group, in which the participants had no idea what others were downloading.

The researchers found that the most popular songs in the control group — a ranking that depended on the merits of the songs themselves, not on what other people were downloading — weren't necessarily popular in the eight social groups.



In many sports, including soccer, the PDO statistic can be used to assign a value to how lucky players and teams are. So while fans like the ones above might chalk a loss up to lack of skill, luck does come into play.

In fact, the song rankings in these eight groups varied wildly. Although the "best" songs usually racked up some downloads, mass popularity wasn't guaranteed.

Instead, fame developed in two stages. First, randomness influenced which tracks people picked early on. The popularity of these first downloaded tracks was then amplified by social behavior, with people looking at the rankings and wanting to imitate their peers.

Mark Roulston and David Hand, statisticians at the hedge fund Winton Capital Management, point out that the randomness of popularity may also influence investment funds' rankings. "Consider a set of funds with no skill," they wrote in 2013. "Some will produce decent returns simply by chance and these will attract investors, while the poorly performing funds will close and their results may disappear from view. Looking at the results of those surviving funds, you would think that on average they do have some skill."

The line between luck and skill — and

**If we want to separate luck and skill in a given situation, we must first find a way to measure them.**

between gambling and investing — is rarely as clear as we think. Lotteries should be textbook examples of gambling, but after several weeks of rollovers, they can produce a positive expected payoff: Buy up all the combinations of numbers, and we'll make a profit.

Sometimes the crossover happens the other way, with investments being more like wagers. Take Premium Bonds, a popular form of investment in the United Kingdom. Rather than receiving a fixed interest rate as with regular bonds, investors in Premium Bonds are entered into a monthly prize draw. The top prize is 1 mil-

lion pounds, tax-free, and there are smaller prizes, too. By investing in Premium Bonds, people are, in effect, gambling the interest they would have otherwise earned. If they instead put their savings in a regular bond, withdrew the interest and used that money to buy rollover lottery tickets, the expected payoff wouldn't be that different.

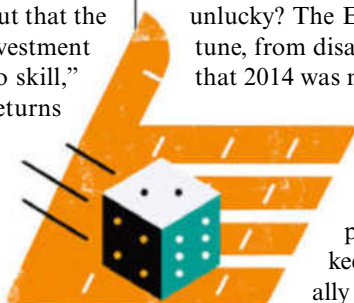
### LUCK AS A STATISTIC

If we want to separate luck and skill in a given situation, we must first find a way to measure them. But sometimes an outcome is sensitive to small changes, with seemingly innocuous decisions completely altering the result. Individual events can have dramatic effects, particularly in sports like soccer and ice hockey, where goals are rare. It might be an ambitious pass that sets up a winning shot or a puck that hits the post. How can we distinguish between a hockey victory that's mostly down to talent and one that benefitted from lucky breaks?

In 2008, hockey analyst Brian King suggested a way to measure how fortunate a particular NHL player is. "Let's pretend there was a stat called 'blind luck,'" he said. To calculate his statistic, he took the proportion of total shots that a team scored while that player was on the ice and the proportion of opponents' shots that were saved, and then added these two values together. King argued that although creating shooting opportunities involved a lot of skill, there was more luck influencing whether a shot went in or not. Worryingly, when King tested the statistic on his local NHL team, it showed the luckiest players were getting contract extensions while the unlucky ones were being dropped.

The statistic, later dubbed "PDO" after King's online moniker, has since been used to assess the fortune of players — and teams — in other sports, too. In the 2014 World Cup, several top teams failed to make it beyond the preliminary group stage. Spain, Italy, Portugal and England all fell at the first hurdle. Was it because they were lackluster or unlucky? The England team is famously used to misfortune, from disallowed goals to missed penalties. It seems that 2014 was no different. England had the lowest PDO of any team in the tournament, with a score of 0.66.

We might think teams with a very low PDO are just hapless. Maybe they have a particularly error-prone striker or a weak keeper. But teams rarely maintain an unusually low (or high) PDO in the long run. If we





analyze more games, a team's PDO will quickly settle down to numbers near the average value of 1. It's what Francis Galton called "regression to mediocrity" — if a team's PDO is noticeably above or below 1 after a handful of games, it's likely due to luck.

## SKILL AS A STATISTIC

Statistics like PDO can be useful to assess how lucky teams are, but they aren't necessarily helpful when placing bets. Gamblers are more interested in making predictions. In other words, they want to find factors that reflect ability rather than luck. But how important is it to actually understand skill?

Take horse races. Predicting events at a racetrack is a messy process. All sorts of factors could influence a horse's performance in a race, from past experience to track conditions. To pin down which factors are useful, syndicates need to collect reliable, repeated observations about races. Hong Kong was the closest American gambler Bill Benter could find to a laboratory setup, with the same horses racing on a regular basis on the same tracks in similar conditions.

Using his statistical model, Benter identified factors that could lead to successful race predictions. He found that some came out as more important than others. In his early analysis, for example, the model said that the number of races a horse had previously run was a crucial factor when making predictions. In fact, it was more important than almost any other factor. Maybe the finding isn't all that surprising. We might expect horses that have run more races to be used to the terrain and less intimidated by their opponents.

It's easy to think up explanations for observed results. Given a statement that seems intuitive, we can convince ourselves why that should be the case, and why we shouldn't be surprised at the result. This can be a problem when making predictions. By creating an explanation, we're assuming that one process has directly caused another. Horses in Hong Kong win *because* they are familiar with the terrain, and they are familiar with it *because* they have run lots of races. But just because two things are apparently related — like probability of winning and number of races run — it doesn't mean that one directly causes the other.

An often-quoted mantra in the world of statistics is that "correlation does not imply causation." Take the wine budget of Cambridge colleges. It turns out that the amount of money each Cambridge college spent on wine in the 2012-2013 academic year was positively correlated with students' exam results during the same period. The more the colleges spent on wine, the better the results generally were.

Similar curiosities appear in other places, too. Countries that consume lots of chocolate win more Nobel prizes. When

ice cream sales rise in New York, so does the city's murder rate. Of course, buying ice cream doesn't make us homicidal, just as eating chocolate is unlikely to turn us into Nobel-quality researchers, and drinking wine won't make us better at exams.

In each of these cases, a separate underlying factor could explain the pattern. For Cambridge colleges, it could be wealth, which would influence both wine spending and exam results. Or a more complicated set of reasons could lurk behind the observations. This is why Benter doesn't try to interpret why some factors appear to be so important in his horse racing model. The number of races a horse has run might be related to another hidden factor that directly influences performance.

Alternatively, there could be an intricate trade-off between races run and other variables — like weight and jockey experience — which Benter could never hope to distill into a neat



To measure skill in horse racing, gambler Bill Benter studied the Hong Kong circuit, which often had the same horses regularly running the same tracks in similar conditions. He found that the number of races a horse ran was the biggest factor in predicting if it would win.

**An often-quoted mantra in the world of statistics is that "correlation does not imply causation."**

"A causes B" conclusion. But Benter is happy to sacrifice elegance and explanation if it means having good predictions. It doesn't matter if his factors are counterintuitive or hard to justify. The model is there to estimate the probability a certain horse will win, not to explain why it will win.

From hockey to horse racing, sports analysis methods have come a long way in recent years. They have enabled gamblers to study matches in more detail than ever, combining bigger models with better data. As a result, scientific betting has moved far beyond card counting. **D**

Excerpt from *The Perfect Bet: How Science and Math Are Taking the Luck Out of Gambling* by Adam Kucharski. Available from Basic Books, a member of The Perseus Book Group. Copyright © 2016.



# Why Are Gray Whales Moving to the Ocean Next Door?

For the first time in thousands of years, the massive creatures of the Pacific are finding their way across the Arctic to the North Atlantic. But trouble may await them.

BY RICHARD SCHIFFMAN

➔ In 2010, when marine biologist Aviad Scheinin posted a photo online of a gray whale off the coast of Israel, his fellow scientists weren't buying it. "Nice Photoshopping," one researcher responded. "Is this April Fools'?" another replied.

Their skepticism was understandable. The species had not been seen outside the Pacific Ocean since the 18th century, when whalers are thought to have harpooned the last Atlantic gray whale. But in 2013, another was spotted even farther afield, off the Atlantic coast of Namibia in southern Africa, where it lingered for a month before swimming off.

Until recently, the Arctic's wall of sea ice made such polar ocean-hopping impossible. Whales need to surface every few minutes to breathe and cannot venture under frozen seas. But increasingly warmer summer temperatures are melting the ice of the Bering Strait and Northwest Passage,



This 2010 photo of a gray whale off the coast of Israel surprised marine biologists, who believed the species was confined to the Pacific Ocean.



Climate change has shrunk the vast sheet of ice covering the Arctic, opening new passageways for gray whales to reach their ancestral home in the Atlantic.

FROM TOP: AVIAD SCHEININ/ISRAELI MARINE MAMMAL RESEARCH AND ASSISTANCE CENTER; ROGER HALL/SCIENCE SOURCE; NASA/GODDARD SPACE FLIGHT CENTER/SCIENTIFIC VISUALIZATION STUDIO





**Top:** Biologist Elizabeth Alter examines a gray whale subfossil for clues to the animal's past. **Right:** Biologist Michael Hofreiter, who worked with Alter, studies narwhal bones.



## WHALES ON THE MOVE

Every year, the nomadic grays take two to three months to swim from the lagoons of Baja California, where they breed and nurse their young, to the feeding grounds off the coast of Alaska. It's one of the longest migrations of any mammal, a round-trip trek of nearly 12,000 miles every year. Once in northern seas, the whales plow the bottom mud and strain

it through flexible baleen plates for tiny, shrimplike creatures and tube worms, fattening up each summer for the return journey south.

But as temperatures rise, these age-old patterns are changing

fast. The timing of the migration has shifted: The whales are leaving their calving grounds earlier and coming back later. Their feeding grounds move steadily north, and evidence suggests some even spend the winter there. And the whales are beginning to feed at various depths as well as along the sea floor, a shift that may have to do with changes in the population densities of their prey.

Even against the backdrop of these changes, the 2010 and 2013 sightings in the Atlantic took biologists by surprise. Those first two gray whale pioneers, which threaded their way through the icy labyrinth of the Northwest Passage into the North Atlantic, accomplished this feat by dumb luck, according to Alter. But now, with the ice receding farther every summer, she says, "the current trickle of strays may turn into a steady stream," though that could take decades or even centuries.

How will these colonizers fare in the Atlantic after all this time? The best guess comes from past population patterns. For years, Alter and her colleagues have meticulously reconstructed the history of the species using subfossils — ancient bones that,

unlike true fossils, are not yet fully mineralized and still contain minute traces of DNA.

Extracting genetic material from these ancient bones is a meticulous practice. At the American Museum of Natural History in New York, where Alter is a research associate, she pauses by a wall of steel shelving in the museum's cavernous basement. It holds ribs the size of small logs and 6-foot-long mandibles — modern bones similar to the subfossils Alter has studied. She points to a black smudge discoloring the surface of a flanged whale vertebra. "We scrape

**"Both the physical ocean and the life within it are shifting much more rapidly than our models predicted for the Arctic," says Elizabeth Alter, a biologist with City University of New York.**

off this dark material, which contains traces of bacterial DNA," she explains. "Then we drill out a tiny wedge of spongy bone matrix and grind it into a fine powder that we use to extract the DNA in the lab."

That DNA was hard-won. When Alter first had the idea to trace the history of gray whales from subfossils in the early 2000s, she quickly hit a major snag; gray whale subfossils are hard to come by. Most lay widely scattered on the bottom of the sea. With little material to work with, the project languished for a year.

Then in 2005, she met evolutionary biologist Michael Hofreiter, then at

opening a water highway between the Pacific and the Atlantic.

If gray whales do migrate to the ocean next door, they'll find that a lot has changed in the Atlantic since the species last plied its waters, including increased ship traffic and higher temperatures. At the same time, says biologist Elizabeth Alter of the City University of New York, these 40-ton bulldozing bottom feeders could have an oversized impact on their new home — for good and for ill.

"Both the physical ocean and the life within it are shifting much more rapidly than our models predicted for the Arctic," Alter notes, adding that temperatures there are rising twice as fast as everywhere else on the planet.

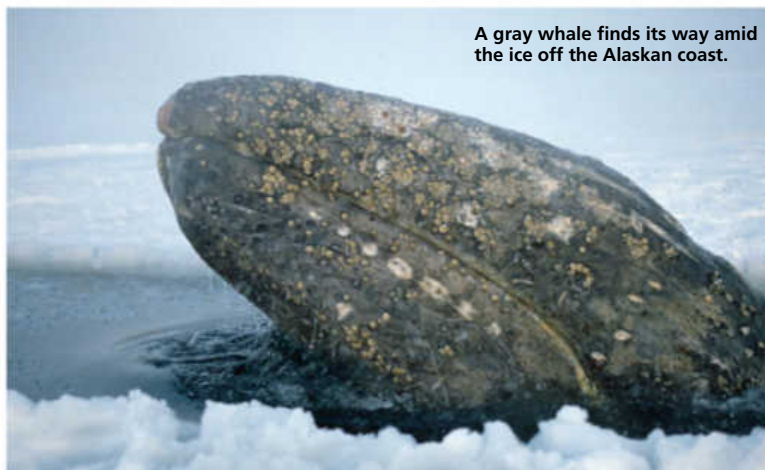
A full-on return to the Atlantic would be an evolutionary homecoming for the species; gray whales lived in the Atlantic for thousands of years. Alter believes traces of these gray whale ancestors hold hints of the species's future. In determining how gray whales responded to historical shifts in the environment, she may be able to help chart what lies ahead for this sensitive "indicator species" — as well as the larger ecosystem.

the Max Planck Institute for Evolutionary Anthropology, who shared some extraordinary news: Dutch trawlers raking the mud of the North Sea dredged up a cache of gray whale subfossils, the largest ever discovered. “I almost fell out of my chair,” Alter recalls. She and Hofreiter teamed up to tease out the story hidden within their new trove.

“Now, for the first time, there was enough material to conduct a really thorough study,” Alter says.

Analyzing this Atlantic material and comparing it with DNA from the Pacific from the same time period, Alter and Hofreiter discovered that grays moved freely between the Pacific and the Atlantic on at least three separate occasions during the late Pleistocene and the Holocene, periods when temperatures were warmer and sea ice was light. (The most recent migratory “pulse” ended about 5,000 years ago.) And based on the genetic diversity in the samples, Alter’s team estimated in 2007 that the archaic population was three to five times larger than it is today.

Nicholas Pyenson, curator of fossil marine mammals at the Smithsonian



A gray whale finds its way amid the ice off the Alaskan coast.

## Researchers found that gray whales moved freely between the Pacific and the Atlantic on at least three separate occasions during the late Pleistocene and the Holocene epochs.

Institution, reached a similar conclusion after analyzing earlier gray whale fossils from the Pleistocene. Not only are gray whales no strangers to the Atlantic, it seems they’ve thrived there under warmer conditions.

### AN UNCERTAIN FUTURE

These insights into the gray whale’s past have left researchers guardedly hopeful about their future. Gray whales are accustomed to traveling far and exploring new areas. And throughout their long history, grays have been “generalists,” not tied to only one food source or feeding method. While they’re sensitive to change, they are also, it turns out, quite resourceful in

responding to it. “They’re a good example of a species that will likely adapt to global climate change better than other less behaviorally flexible whales,” Pyenson says.

But the Atlantic today is different from the ocean the grays once swam in. The whales that return to their

ancestral home will have to cope with a greater risk of fatal collisions with ships than in the Pacific. They may have to dodge oil- and gas-drilling operations in the Arctic and the North Atlantic as well as deafening sonar blasts. And as the climate changes, their food sources, from phytoplankton to tiny crustaceans, may shrink.

The whales, in turn, could affect their new neighborhood if they arrive in large numbers. Like beavers, gray whales are ecosystem engineers whose activities transform the places where they live. They stir up enormous plumes of mud while bottom-feeding, for instance. But just what effect they’ll have is unknown.

Studying the ancient DNA of gray whales has opened a new door into how ecosystems have changed over time — and underscores the unprecedented pace of change in today’s human-altered world, Alter says.

“With human-caused climate change, we’re running a vast, unintended ecological experiment,” she says. “We simply can’t say yet what the results are going to be. But it is clear that the consequences for gray whales — and for the oceans they inhabit — will last well beyond our lifetimes and our children’s lifetimes.” **D**

*Richard Schiffman is a widely published environmental journalist, a poet and the author of two biographies.*



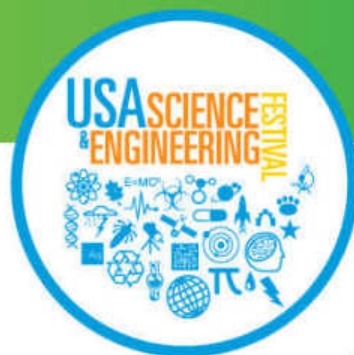
A female gray whale and her calf ply the waters of San Ignacio Lagoon in Baja California Sur, Mexico, a primary breeding ground and nursery.



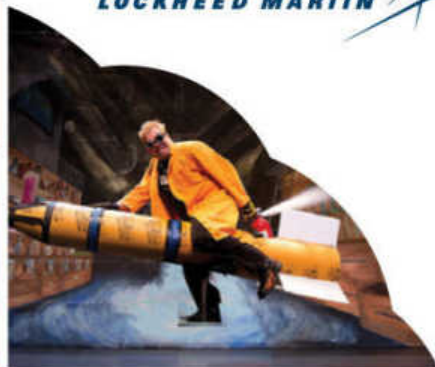
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## A Cosmos, Darkly

After eight decades, most of the universe is still missing from view, forcing astronomers to abandon the notion that seeing is believing.

BY COREY S. POWELL

→ Often in science it takes a long time to understand exactly how confused you are. Nobody knew to wonder how the dinosaurs went extinct, for instance, until 19th-century fossil diggers realized that dinosaurs had existed in the first place. In the case of dark matter — the unseen *something* that seems to make up about five-sixths of the matter in the universe — the confusion has been building for a good 84 years, and shows no sign of going away.

That's not how it was supposed to be. A few years ago, various instruments seemed hot on the trail of the unseen cosmic component. In space, the orbiting Fermi Gamma-ray Space Telescope detected possible

hints of dark matter particles breaking down into visible components. In an Italian laboratory, an international team claimed provocative evidence of a seasonal “wind” of dark matter blowing through its specially designed detector, called DAMA. And 4,850 feet underground, in an abandoned South Dakota gold mine, the enormous Large Underground Xenon (LUX) dark matter detector geared up to collect the definitive data on the long-sought dark particles.

But instead of enlightenment, what followed was a new wave of confusion. The Fermi signal looked like a mix of known astrophysical processes and random galactic noise. The DAMA results did not match up with data

Dark matter, whatever it may be, abounds throughout galaxy cluster Abell 2744. In this visualization, dark matter appears blue; galaxies, white; and hot gas, red.

from other detectors, and so aroused widespread skepticism. As for LUX, it was a huge success — just in a negative way. It delivered a high-quality null result, the scientists' way of saying that they found exactly zero evidence for a great many of the hypothesized or allegedly detected dark matter particles.

Science, like nature, abhors a vacuum, so a variety of new theories have whooshed into the void. Perhaps dark matter is bunched together into large, elusive clumps; perhaps it interacts with ordinary matter even less than physicists expected. Dark matter is so peculiar and puzzling that it has



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inspired far-grasping speculations even from sober-minded researchers. Harvard physicist Lisa Randall has just published an entire book exploring the argument that dark matter might have indirectly killed the dinosaurs.

This all sounds a bit like chasing unicorns — indeed, cheeky grad students have placed little paper unicorns all around the LUX facility — except for one huge, exciting, maddening fact: Dark matter really exists.

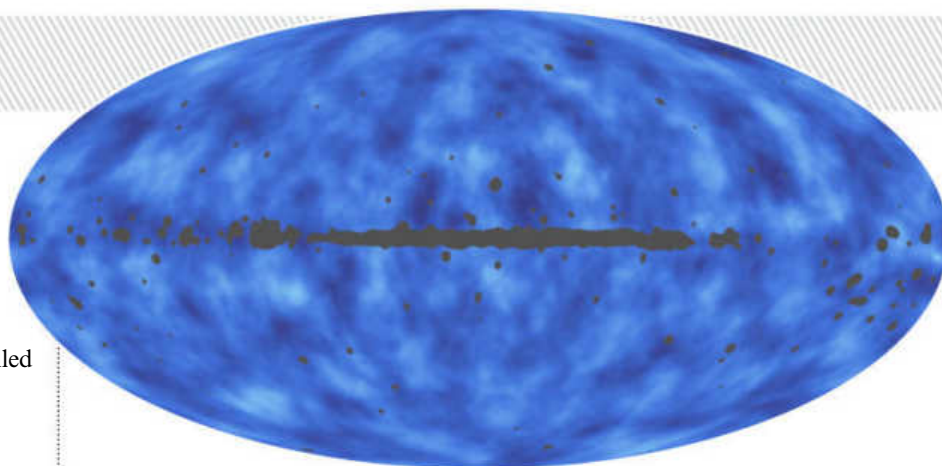
## EVIDENCE OF INVISIBILITY

You may well ask how I can say that with such certainty. In fact, many of you *do* ask, on Twitter, Facebook and online comments sections. The question deserves a serious answer.

The case for dark matter began in the 1930s with a pair of papers by two very different kinds of geniuses, the buttoned-down Dutch astronomer Jan Oort (who also hypothesized the Oort Cloud of comets) and the explosive Swiss-American cosmologist

Fritz Zwicky. Oort noted that the motions of stars within our galaxy imply the presence of a great deal of additional unseen, dark material. Zwicky took the argument further, noting that entire clusters of galaxies would scatter unless bound together by the gravitational pull of more invisible stuff.

Oort and Zwicky were working with limited data, yet their conclusions proved remarkably robust. In the 1970s, astronomers Vera Rubin and Kent Ford used the same basic arguments to show, in much more convincing detail, that spiral galaxies appear to keep their shapes because of the gravitational glue from



The Planck mission created this all-sky map in 2015 showing matter in the universe. (More massive regions are darker, with our galaxy grayed out.) Dark matter makes up the vast bulk.

**Only about one-sixth of the deduced mass of the galaxy clusters can consist of atoms. Not only is most of their matter dark, then, but the dark matter simply cannot be the same kind of stuff we are made of.**

nearby dark matter.

Once their colleagues started taking the idea seriously, they saw dark matter everywhere: Almost every aspect of the formation, motion and clustering of galaxies indicates the presence of far more mass than can be accounted for by the visible stars and nebulae.

At this point, the case turns even more interesting and complicated. Theoretical models of the Big Bang allow precise calculations of the composition of the early universe. Those calculations, in turn, indicate the precise amount of ordinary matter expected in the universe. During the 1980s, researchers plugged the numbers into

their computers and out came a hard prediction: Only about one-sixth of the deduced mass of the galaxy clusters can consist of atoms. Not only is most of their matter dark, then, but the dark matter simply cannot be the same kind of stuff we are made of.

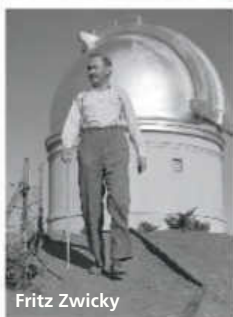
Starting in the 1990s, studies of the cosmic microwave background (the afterglow of the Big Bang) offered a different test of this startling idea. Reverberations in the very young universe imprinted onto that background a discernible pattern, which depends on the mix of ordinary matter to dark matter. In 2013, the Planck satellite gave the definitive reading on that mix. The result, again: one-sixth ordinary matter, five-sixths dark matter.

But wait, there's more! Because dark matter does not interact with radiation (if it did, we could see its light), it can clump together more efficiently than atoms, which tend to heat up and get agitated. The efficient clumping of dark matter allowed it to create dense patches that spurred the formation of the first galaxies. Put dark matter into the models, and they can pretty much explain the structure of the modern universe. Without dark matter, the models fail miserably.

A few researchers, most notably Mordehai Milgrom at the Weizmann Institute in Israel, have perceived a possible flaw in these deductions. Almost all the evidence for dark matter ultimately depends on its gravitational effects. Perhaps the reason the universe



Jan Oort



Fritz Zwicky

In the 1930s, scientists Oort and Zwicky were early pioneers in the case for dark matter.





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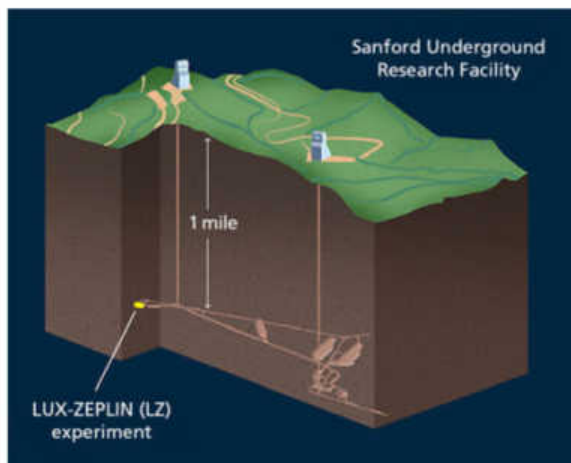
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About a mile underground in a South Dakota cavern, the LUX experiment looked for, and didn't find, dark matter particles. Starting in 2019, the much more sensitive LUX-ZEPLIN might have better luck. At right, a technician inspects LUX's 6-foot liquid xenon tank, housed within a yet-to-be-filled water chamber.



looks strange is not because of dark matter, but because the standard theory of gravity is slightly wrong, Milgrom suggests.

The problem with his argument is that no single modification of gravity can explain all the different phenomena outlined above. Making everything fit requires a new theory of gravity, plus additional undiscovered long-range forces, and still requires some exotic dark matter on top of that. There is no escaping the dark truth.

## FROM DARKNESS, LIGHT

Dark matter is not a hunch, nor is it some kind of scientific sleight of hand. It is an actual, physical thing discovered indirectly but definitively based on multiple independent lines of evidence.

That evidence leaves astronomers in an uncomfortable place, with the vast majority of the cosmos missing. Fortunately, the current situation still leaves a lot more places to investigate. After the LUX experiment completes its run, the affiliated researchers will regroup to build an upgraded version called LUX-ZEPLIN (nerd band name alert), or LZ, which will be 10 times as large and sensitive. In the meantime, a competing team is upgrading a

**It's possible that both approaches will fail. Then the process of finding dark matter becomes exponentially harder, though not necessarily impossible.**

device called the Axion Dark Matter eXperiment (ADMX), which will search for axions, a hypothetical dark particle so slight that it would sail right through LUX undetected.

It's possible that both approaches will fail. Then the process of finding dark matter becomes exponentially harder, though not necessarily impossible. Dark matter particles might occasionally destroy each other, creating a visible signal (like the now-discredited Fermi observation). Or they might interact with each other to produce organized structures, such as a thin, dark disk embedded within our galaxy. A dark disk could have an ominous effect, gravitationally destabilizing our solar system every

30 million years or so and setting loose a rain of comets. Such a comet shower could potentially trigger a mass extinction — hence Randall's link between dark matter and dinosaurs.

A variety of sky surveys, from both space and terrestrial observatories, are seeking dark structures in our galaxy and beyond. Whether or not they confirm Randall's specific model of dark matter, those surveys will provide a lot more information about how the dark stuff behaves and what it might consist of. They will provide a more accurate cosmic map of all matter, both the seen and the unseen. Above all, Randall says, the ongoing study of dark matter is a precious exercise in "exploring connections" — not just between different fields of science, but also between humans and the cosmos.

As much as it is a source of confusion, dark matter is also a source of illumination. It is all around us. It is almost surely passing through you right now. Our galaxy would not exist without it. We literally owe it our lives. **D**

**Corey S. Powell**, a contributing editor of *Discover*, also writes for the magazine's *Out There* blog. Follow him on Twitter, @coreypowell





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# Coming to Paleo-America

Genetic studies resolve long-standing debates about who first settled our continent — but pose new questions.

BY ZACH ZORICH

➤ The archaeological evidence left behind by the first people to settle the Americas tells a confusing story. Researchers have long understood that people migrated from Siberia to Alaska across a region called Beringia, which included a now-submerged land bridge — but they disagree whether the artifacts at Siberian sites resemble those on the other side of the Bering Strait. And the few skulls they’ve found of the earliest Americans don’t look much like those of modern Native Americans.

The sparse and sometimes conflicting data raised questions about who the first settlers of the Americas were, when they arrived and whether other waves of migration followed. The lack of evidence inspired some, shall we say, “esoteric” theories of Paleolithic settlers boating over from France or Polynesia. “For a while, everybody could [seem] right,” says Ted Goebel, an archaeologist at Texas A&M University who has worked at sites on both sides of the Bering Strait. Goebel is also co-author of a 2015 study published in *Science* that brings together genetic and archaeological data to end speculation.

The study, led by Eske Willerslev, an evolutionary geneticist at the University of Copenhagen, compared the genomes of three ancient skeletons — a 24,000-year-old child found in central Siberia, a 12,600-year-old Montana child known as Anzick-1 and a 4,000-year-old Saqqaq Eskimo from Greenland — to the genomes of 31 indigenous people currently living in Asia, North and South America, and the Pacific islands. The results added to a growing body of evidence showing



that all modern Native Americans share ancestry with the Anzick child, and that the majority of all indigenous people in the Americas can trace their lineages back to a single migration that took place about 15,000 years ago.

The research suggests that the people directly ancestral to Native Americans actually split away from their Siberian cousins as early as 23,000 years ago. This population migrated only as far as Beringia at first, because glaciers blocked the way farther eastward into the Americas. Genetic analysis shows

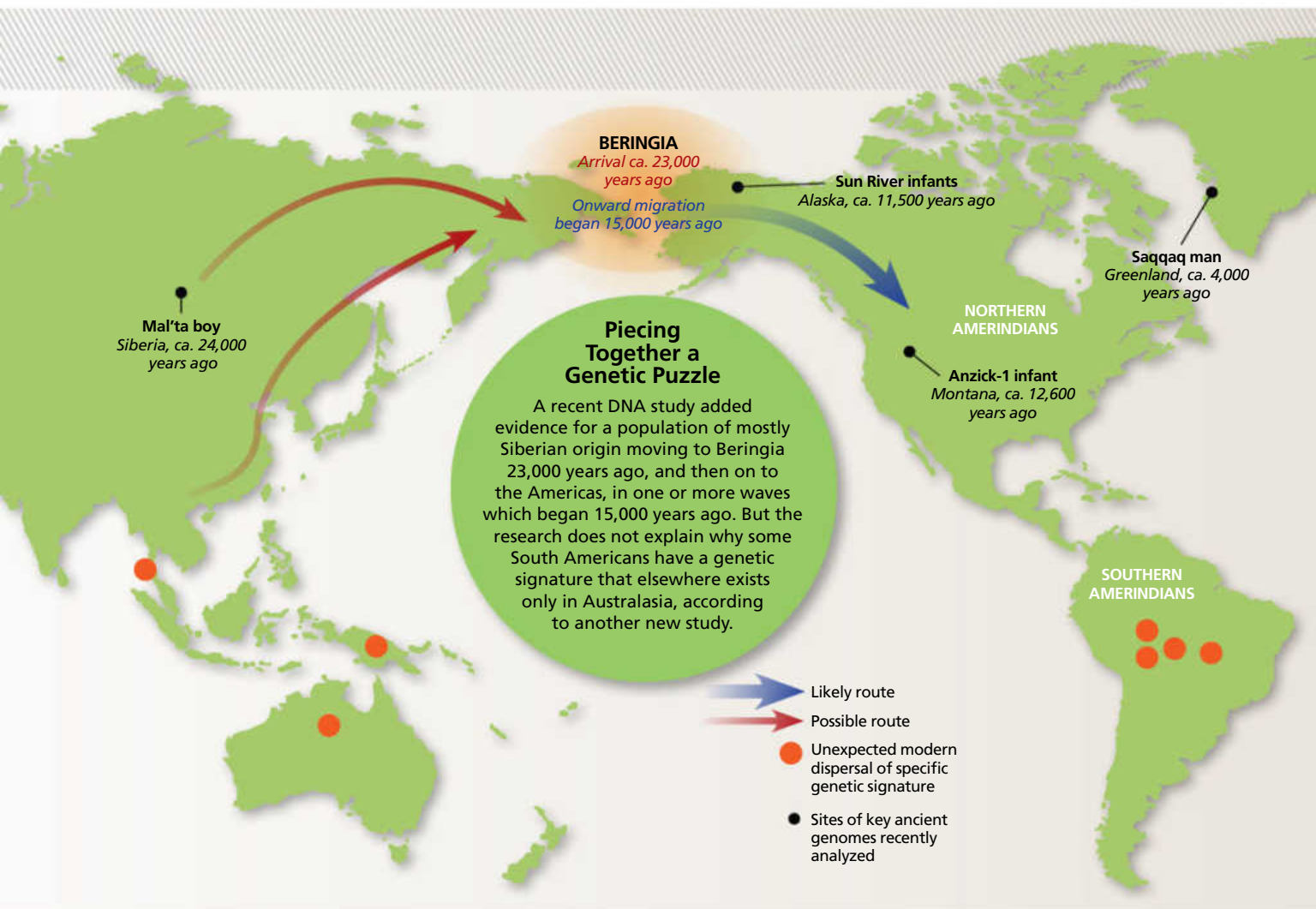
that this Beringian period lasted no longer than 8,000 years before the population pushed into North and, eventually, South America.

That was not the only migration event, however.

## COSMOPOLITAN PAST

“We’re still not entirely sure” how many migrations there were, says Pontus Skoglund, a geneticist at Harvard University. He thinks there were as many as five separate waves and believes there may have been





distinct ethnic groups within the population living in Beringia at the time the Americas were first settled, which could confuse the picture. The lead author of a separate 2015 study in *Nature*, Skoglund looked at the genomes of ancient and modern Native Americans. His team's research found that a specific Australasian genetic signature — one found in people who lived in Australia, Indonesia and the Andaman Islands, off the coast of Burma — survives today in some of South America's indigenous people. Skoglund believes this genetic signature is evidence of another, smaller migration that was separate, but possibly concurrent, with the main wave from Beringia.

On its surface, the presence

of Australasian genes might seem to indicate that people had sailed from that area across the Pacific Ocean to the Americas, but that genetic signature does not show up in people in the Pacific islands, which likely would have been along the route.



DNA from the 24,000-year-old Mal'ta boy, found in Siberia in the 1920s, provided clues about the origins of the first Americans.

Unlike Skoglund, Willerslev believes that this signature was brought by a group of people who migrated via Beringia, or possibly boated along the coast from Siberia to South America, around 13,000 years ago — a couple of thousand years after the initial, larger migration.

The debate comes down to how each team interprets the genetic data. For now, the ancient Siberian genome also analyzed in the *Science* study supports the idea of a highly genetically diverse population living in Siberia prior to migration into the Americas. The 24,000-year-old Siberian individual who was sequenced had ancestry in common with people in Europe, which shows that these Paleolithic

hunter-gatherers were moving over a larger territory than had been assumed. In October, a separate study of the maternally inherited mitochondrial DNA of the remains of two Alaskan children, dated to 11,500 years ago, revealed that one child had a rare genetic signature found on the southern edge of Siberia. These studies showing greater genetic diversity in ancient populations suggest it may not be so far-fetched to think that Siberians could have come into contact with people carrying Australasian genes, and then taken those signatures to the Americas over subsequent generations.

“What we really see is that it was a lot more cosmopolitan back then,” says Maanasa Raghavan, a geneticist at the Natural History Museum of Denmark and part of the team behind the *Science* study.

Curiously, the subsequent possible migrations that Skoglund references — unrelated to the wave that brought Australasian genetic signatures to our shores — don’t seem to have progressed beyond northern North America. The most recent migration backed by genetic and archaeological evidence, for example, occurred only 700 years ago: The Thule Inuit people spread out from the Bering Strait region across the Arctic, replacing the Paleo-Eskimo people who had lived there for millennia.

## HOMEGROWN DIVERSITY

The genetic studies provide greater context for archaeological evidence found in the Americas: The research shows that the incredible diversity of cultures and languages among the native people of the Americas developed in place. It was not the result



After sequencing the DNA of 8,500-year-old Kennewick Man, researchers concluded he is related to all modern Native Americans.

**The studies strengthen the case that all indigenous Americans descended from the first inhabitants, which could resolve some legal limbos.**

of new groups of people bringing new artifacts or belief systems from outside, as has sometimes been theorized.

The studies also strengthen the case that all of the indigenous people living in the Americas descended from the continents’ first inhabitants, which

could resolve a legal limbo for some archaeological artifacts and human remains.

Consider, for example, the decades-long custody battle over an 8,500-year-old skeleton known as Kennewick Man, found in Washington state. Local Native American tribes have been fighting to rebury the remains as those of a direct ancestor, in accordance with a federal law. But researchers argued they had the right to study the skeleton based on the skull’s features, which differed from those of modern Native Americans — thus suggesting Kennewick Man was not an ancestor. Willerslev’s team, in a separate 2015 study, was able to sequence Kennewick Man’s DNA and confirm he was, in fact, related to all Native Americans. As for the disparity in skull features, a number of factors, including diet and random genetic drift, could account for differences in appearance between modern Native Americans and Kennewick Man. Those same factors may also explain

more generally how the skull shapes of indigenous American populations changed over millennia.

The growing number of ancient and modern genomes available for study continues to refine our understanding of how the Americas were settled. Old school fieldwork is also part of the process: Goebel, for example, is looking forward to excavating sites in Alaska that might challenge or augment the migration models created with genetic data. “Some of the stories are being majorly rewritten,” says Raghavan. “We know we’re not done yet; we’ve got a lot more to go.”

*Zach Zorich is a freelance journalist who recently migrated to Colorado.*



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## 20 Things You Didn't Know About ...

# Marijuana

BY GEMMA TARLACH



**1** Pot. Weed. Mary Jane. Sticky-icky. Nicknames aside, much of the world calls the psychotropic plant by its scientific name, *cannabis*, and — until the early 20th century — so did Americans. **2** About a hundred years ago, however, the term *marijuana* became common in the United States, the result of anti-cannabis, anti-immigrant advocates trying to link recreational use of the plant to migrant workers from Mexico. **3** The American groups rallying against both the plant and the people they distrusted borrowed a term — *marihuana* — that came to prominence first in Mexico. **4** The word *marijuana* and all its spelling variants, however, may not have Latin American roots. Some researchers have argued the word originated in China, where *ma ren* and *ma hua* refer to different parts of the plant. **5** Still other etymologists lobby for an Arabic origin of the word, which may have arrived in Mexico via Moorish Spain. **6** Whatever you call it, cannabis originated in Asia, though researchers of a landmark 2015 genetic analysis of the plant noted its evolutionary history “remains poorly understood.” **7** We do know that humans have been cultivating cannabis for at least 6,000 years and possibly twice that long, which would make it one of our earliest crops. **8** The first evidence of the plant’s cultivation comes from East Asia, where the stems were used for fibers and the fruits eaten. But cannabis is also mentioned in the *pen-ts’ao ching*, the world’s oldest pharmacopoeia, which was compiled from Chinese oral traditions dating back to 2700 B.C. **9** According to the ancient text, cannabis was used to relieve conditions ranging from constipation to malaria, though its hallucinogenic qualities also were noted. **10** Many other early cultures took advantage of the plant’s psychotropic and medicinal effects, notably in India, where cannabis was considered one of five sacred plants. **11** Cannabis is also mentioned in the Talmud, Judaism’s key ancient text, and evidence of its pollen or oil has been found in several ancient Egyptian tombs, including that of the pharaoh Ramses II. **12** The nomadic Scythians, whom Greek historian Herodotus documented using cannabis in funereal rites in 450 B.C., likely introduced the plant to Europe. **13** But *what* plant, exactly? Historical and cultural divisions between different species in

the genus *Cannabis* get messy. Just ask the authors of that 2015 genetic study, who found commercially cultivated plants described as the species *C. sativa* were sometimes actually *C. indica*, genetically speaking, or vice versa. **14** The confusion over which strain belongs to which species derives in part from illicit growers ascribing a species name to a plant based on its psychotropic effects, rather than its actual genetic makeup: Many, ah, *enthusiasts* believe *C. sativa* produces a stimulating, mind-altering effect thanks to delta-9-tetrahydrocannabinol (THC), a chemical found in the plant’s sticky resin. **15** These non-scientific aficionados also claim anecdotally that *C. indica* acts more like a sedative because it has a greater proportion of cannabidiol (CBD) than THC. The popular notions are misguided: Both species are typically high in THC and low in CBD. Differing psychotropic effects are more likely due to other chemicals in the resin. **16** CBD, an anti-inflammatory, is considered the most useful active substance for medical marijuana use. In 2011, Israeli researchers bred a strain of the plant loaded with CBD specifically for therapeutic use. **17** Regardless of strain, researchers have long thought the female plant produces the sticky resin, full of cannabinoids including THC and CBD. Recent studies suggest, however, that male and female plants may produce cannabinoids equally. **18** Recreational marijuana use is notoriously associated with the munchies, or junk food cravings, but a 2014 study documented that long-term ingestion of the plant caused mice to eat less and lose weight — at least in a lab setting, without access to Doritos or doughnuts. **19** Another surprise: Although some researchers in the past have described the non-psychotropic variety of the plant, commonly known as hemp, as the subspecies *Cannabis sativa* L., it’s actually more closely related to *C. indica*. Dividing *Cannabis* into species and subspecies remains a sticky issue with little agreement among researchers. **20** Except when it comes to *C. ruderalis*. Consensus about the uncommon and possibly feral *Cannabis* species is that it’s of little value for recreational or medical use. So *don’t* put that in your pipe and smoke it. **D**

Senior Editor **Gemma Tarlach**’s drug of choice is caffeine.

The focus of much current debate, marijuana may be one of our oldest crops.

DISCOVER (ISSN 0274-7529, USPS# 555-190) is published monthly, except for combined issues in January/February and July/August. Vol. 37, no. 3. Published by Kalmbach Publishing Co., 21027 Crossroads Circle, P.O. Box 1612, Waukesha, WI 53187-1612. Periodical postage paid at Waukesha, WI, and at additional mailing offices. POSTMASTER: Send address changes to DISCOVER, P.O. Box 62320, Tampa, FL 33662-2320. Canada Publication Agreement # 40010760. Back issues available. All rights reserved. Nothing herein contained may be reproduced without written permission of Kalmbach Publishing Co., 21027 Crossroads Circle, P.O. Box 1612, Waukesha, WI 53187-1612. Printed in the U.S.A.



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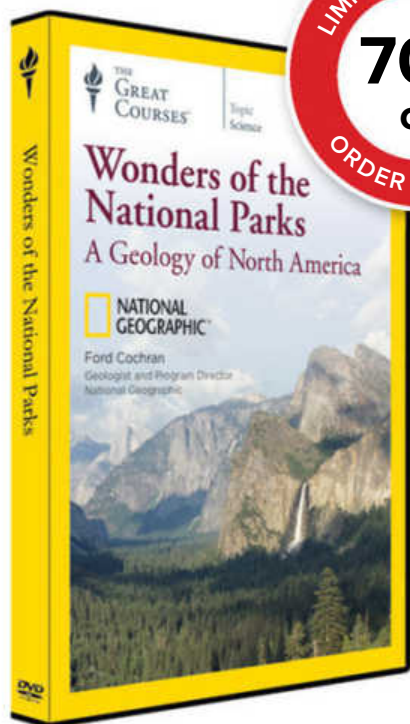
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